

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	872	((gene adj express\$) near5 (profil\$ or pattern\$)) near20 correlat\$	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:20
L2	2742	((gene adj express\$) near5 (profil\$ or pattern\$)) near20 compar\$	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:21
L3	3202	I1 or I2	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:21
L4	41623	435/6[ccls]	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:29
L5	1700	I3 and I4	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:30
L6	1327347	@rlad<"20040225"	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:31
L7	1019	I5 and I6	US-PGPUB; USPAT; EPO; JPO; DERWENT; IBM_TDB	OR	ON	2007/08/03 16:31

Serial No. 10/590,256

Please scan these and index them as

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James Martinell  
Primary Examiner 1634

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1150172 EXPRESS?/BI 1074597 EXPRESS?/AB  
405799 PROFIL?/BI 370131 PROFIL?/AB  
674022 PATTERN?/BI 637269 PATTERN?/AB  
L1 23977 ((GENE#(W)EXPRESS?)(5A)(PROFIL? OR PATTERN?))/BI,AB

=> s correlat?/bi,ab 977001 CORRELAT?/BI  
924425 CORRELAT?/AB  
L2 977001 CORRELAT?/BI,AB

=> s l1 and l2  
L3 2425 L1 AND L2

=> s (test? or assay?)/bi,ab 1814289 TEST?/BI  
1685280 TEST?/AB 496830 ASSAY?/BI  
450062 ASSAY?/AB  
L4 2208064 (TEST? OR ASSAY?)/BI,AB

=> s l3 and l4  
L5 539 L3 AND L4

=> s (expression(w)profil?)/bi,ab 799939 EXPRESSION/BI  
699784 EXPRESSION/AB 405799 PROFIL?/BI  
370131 PROFIL?/AB  
L6 24135 (EXPRESSION(W)PROFIL?)/BI,AB

=> s l5 and l6  
L7 442 L5 AND L6

=> s l7 not 2005/py 810709 2005/PY  
L8 320 L7 NOT 2005/PY

=> s l8 not 2004/py 1260280 2004/PY  
L9 169 L8 NOT 2004/PY

=> d his  
(FILE 'HOME' ENTERED AT 15:40:59 ON 19 SEP 2005)  
FILE 'CAPLUS' ENTERED AT 15:41:09 ON 19 SEP 2005  
L1 23977 S ((GENE#(W)EXPRESS?)(5A)(PROFIL? OR PATTERN?))/BI,AB  
L2 977001 S CORRELAT?/BI,AB  
L3 2425 S L1 AND L2  
L4 2208064 S (TEST? OR ASSAY?)/BI,AB  
L5 539 S L3 AND L4  
L6 24135 S (EXPRESSION(W)PROFIL?)/BI,AB  
L7 442 S L5 AND L6

2 8/3/07

L8 320 S L7 NOT 2005/PY  
L9 169 S L8 NOT 2004/PY

=> d I9 1-169 bib ab

L9 ANSWER 1 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2005:23652 CAPLUS  
DN 142:258908

TI Effect of AKR1C2 gene on hepatocarcinogenesis and its abnormal expression in hepatocellular carcinoma from Qidong, China, a liver cancer high risk area  
AU Lu, Dongdong; Zhang, Xiran; Cao, Xiangrong  
CS College of Life Science, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China  
SO Shengwu Huaxue Yu Shengwu Wuli Jinzhan (2003), 30(6), 906-918 CODEN: SHYCD4; ISSN: 1000-3282  
PB Shengwu Huaxue Yu Shengwu Wuli Jinzhan Bianjibu  
DT Journal  
LA English  
AB Abnormal AKR1C2 expression was obsd. in many malignant human tumors, but its relationship with hepatocellular carcinoma(HCC) is not well understood so far. In order to evaluate hepatocarcinogenic effect of AKR1C2 gene and the significance of its abnormal expression in hepatocellular carcinoma, AKR1C2 gene is analyzed by prepg. rabbit anti-human AKR1C2 polyclonal antibody, constructing of AKR1C2 frame shift mutant and exploring RT-PCR, in situ hybridization, immunohistochem., Western blot, Northern blot, cDNA expression microarray, co-immunopptn. and the tumorigenicity \*\*\*assay\*\*\* in vivo and in vitro etc. AKR1C2 gene expression and its effects was analyzed, including 68 pairs of HCC specimens and its adjacent para-cancerous tissues, 8 cases of normal liver tissues and QGY7703 cell line. Results showed AKR1C2 expression was up-regulated among these patients, when compared with those of para-cancerous and normal liver tissues. Over-expression of AKR1C2 is also found to be \*\*\*correlated\*\*\* with high metastasis potentiality of HCC. AKR1C2 overexpression stimulates DNA synthesis, apoptosis, growth in soft agar and promote tumor formation and lead to expression differences of tumor genes. AKR1C2 mediated the NV-KB-dependent resistance of QGY7703 cells to anti-fas killing. Intraocular binding of AKR1C2 and Cdk4 was found. Abnormal expression of AKR1C2 gene may contribute to the occurrence, advancement and invasiveness of HCC from Qidong, China, a liver cancer high risk area.

L9 ANSWER 2 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:1150473 CAPLUS  
DN 142:153464

TI Role of NFAT transcription factors in regulating integrin-mediated carcinoma invasion and its use in monitoring prognosis and drug screening

IN Toker, Alex; Jauliac, Sebastian  
PA Beth Israel Deaconess Medical Center, USA  
SO Can. Pat. Appl., 97 pp. CODEN: CPXXEB  
DT Patent  
LA English

FAN.CNT 1 PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE		
PI CA 2377172	AA	20031002	CA 2002-2377172
20020402			
PRAI CA 2002-2377172		20020402	

AB The present invention related to the role of NFAT transcription factors in regulating integrin-mediated carcinoma invasion and its use in monitoring prognosis and drug screening.

Here, the authors investigate the involvement of NFAT in promoting carcinoma invasion downstream of the .alpha.6.beta.4 integrin. The authors provide evidence that NFAT is expressed in invasive human ductal breast carcinomas and participate in promoting carcinoma invasion using cell lines derived from human breast. NFAT1, NFAT4 and NFAT5 activity \*\*\*correlates\*\*\* with the expression of the .alpha.6.beta.4 integrin. In addn., the transcriptional activity of NFAT5 is induced by .alpha.6.beta.4 clustering in the presence of chemo-attractants, resulting in enhanced cell migration. These observations show that NFATs are targets of .alpha.6.beta.4 integrin signaling and are involved in promoting carcinoma invasion, highlighting a novel function for this family of transcription factors in human cancer.

L9 ANSWER 3 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:572371 CAPLUS  
DN 141:200855

TI Probabilistic estimation of microarray data reliability and underlying gene expression  
AU Bilke, S.; Breslin, T.; Sigvardsson, M.  
CS Complex Systems Division, Department of Theoretical Physics, University of Lund, Lund, SE-22185, Swed.  
SO Los Alamos National Laboratory, Preprint Archive, Quantitative Biology (2003) 1-12, arXiv:q-bio.QM/0309006, 18 Sep 2003 CODEN: LANLCJ URL: <http://xxx.lanl.gov/pdf/q-bio.QM/0309006>  
PB Los Alamos National Laboratory  
DT Preprint  
LA English

AB The availability of high throughput methods for measurement of mRNA concns. makes the reliability of conclusions drawn from the data and global quality control of samples and hybridization important issues. These issues were addressed by an information theoretic approach, applied to discretized expression values in replicated gene expression data. The approach yields a quant. measure of two important parameter classes: First, the probability  $P(\sigma_i | S)$  that a gene is in the biol. state  $\sigma_i$  in a certain variety, given its obsd. expression  $S$  in the samples of that variety. Second, sample specific error probabilities which serve as consistency indicators of the measured samples of each variety. The method and its limitations are \*\*\*tested\*\*\* on gene expression data for developing murine B-cells and a t- \*\*\*test\*\*\* is used as ref. On a set of known genes it performs better than the t- \*\*\*test\*\*\* despite the crude discretization into only two expression levels. The consistency indicators, i.e. the error probabilities, \*\*\*correlate\*\*\* well with variations in the biol. material and thus prove efficient. The proposed method is effective in detg. differential gene expression and sample reliability in replicated microarray data. Already at two discrete expression levels in each sample, it gives a good explanation of the data and is comparable to std. techniques.  
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:513878 CAPLUS  
DN 141:237255

TI Gene selection for multi-class prediction of microarray data  
AU Chen, Dechang; Hua, Dong; Reifman, Jaques; Cheng, Xiuzhen  
CS Uniformed Services, University of the Health Sciences, Israel  
SO Proceedings of the IEEE Bioinformatics Conference, 2nd, Stanford, CA, United States, Aug. 11-14, 2003 (2003), Meeting

Date 2003, 492-495 Publisher: IEEE Computer Society, Los Alamitos, Calif. CODEN: 69FOVN; ISBN: 0-7695-2000-6  
DT Conference  
LA English

AB Gene expression data from microarrays have been successfully applied to class prediction, where the purpose is to classify and predict the diagnostic category of a sample by its \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\*. A typical microarray dataset consists of expression levels for a large no. of genes on a relatively small no. of samples. As a consequence, one basic and important question assocd. with class prediction is; how do we identify a small subset of informative genes contributing the most to the classification task. Many methods have been proposed but most focus on two-class problems, such as discrimination between normal and disease samples. This paper addresses selecting informative genes for multi-class prediction problems by jointly considering all the classes simultaneously. Our approach is based on the power of the genes is discriminating among the different classes (e.g., tumor types) and the existing \*\*\*correlation\*\*\* between genes. We formulate the expression levels of a given gene by a one-way anal. of variance model with heterogeneity of variances, and det. the discriminatory power of the gene by a \*\*\*test\*\*\* statistic designed to \*\*\*test\*\*\* the equality of the class means. In other words, the discriminatory power of a gene is assocd. with a Behrens-Fisher problem. Informative genes are chosen such that each selected gene has a high discriminatory power and the \*\*\*correlation\*\*\* between any pair of selected genes is low. \*\*\*Test\*\*\* statistics considered in this paper include the ANOVA F \*\*\*test\*\*\* statistic, the Brown-Forsythe \*\*\*test\*\*\* statistic, the Cochran \*\*\*test\*\*\* statistic, and the Welch \*\*\*test\*\*\* statistic. Their performances are evaluated over several classification methods applied to two publicly available microarray datasets. The results show that Brown-Forsythe \*\*\*test\*\*\* statistic achieves the best performance.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2004:366542 CAPLUS  
DN 141:136596

TI Connective molecular pathways of experimental bladder inflammation

AU Dozmorov, Igor; Saban, Marcia R.; Knowlton, Nicholas; Centola, Michael; Saban, Ricardo  
CS Oklahoma Medical Research Foundation, Arthritis and Immunology Research Program, Microarray Core Facility, The University Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA

SO Physiological Genomics (2003), 15(3), 209-222 CODEN: PHGEFP; ISSN: 1094-8341 URL: <http://physiolgenomics.physiology.org/cgi/reprint/15/3/209.pdf>

PB American Physiological Society

DT Journal; (online computer file)

LA English

AB Inflammation is an inherent response of the organism that permits its survival despite const. environmental challenges. The process normally leads to recovery from injury and to healing. However, if targeted destruction and assisted repair are not properly phased, chronic inflammation can result in persistent tissue damage. To better understand the inflammatory process, the authors recently introduced a profiling methodol. to identify common genes involved in bladder inflammation. The method represents a complementation to the classic quantification of

inflammation and provides information regarding the early, intermediate, and late events in gene regulation. However, gene profiling fails to describe the mol. pathways and their interconnections involved in the particular inflammatory response. The present work introduces a new statistical technique for inferring functional interconnections between inflammatory pathways underlying classic models of bladder inflammation and permits the modeling of the inflammatory network. This new statistical method is based on variants of cluster anal., Boolean networking, differential equations, Bayesian networking, and partial \*\*\*correlation\*\*\*. By applying partial \*\*\*correlation\*\*\* anal., the authors developed mosaics of gene expression that permitted a global visualization of common and unique pathways elicited by different stimuli. The significance of these processes was \*\*\*tested\*\*\* from both biol. and statistical viewpoints. The authors propose that connective mosaic may represent the necessary simplification step to visualize cDNA array results. RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2004:199920 CAPLUS  
DN 141:255590

TI Reversible phenotype and a lack of direct link to immortalization of Syrian hamster embryonic cells obtained from so-called transformed colonies

AU Tsuda, Hirohisa

CS Central Pharmaceutical Research Institute, Japan Tobacco Inc., Osaka, 569-1125, Japan

SO Kankyo Hen'igen Kenkyu (2003), 25(3), 159-168 CODEN: KHKEEN; ISSN: 0910-0865

PB Nippon Kankyo Hen'igen Gakkai

DT Journal

LA English

AB The short-term colony transformation \*\*\*assay\*\*\* employing Syrian hamster embryonic (SHE) cells has been widely used as a simple method for detection of chem. and phys. carcinogens. However, little investigation has been done on the biol. properties of the early transformed colony (ETC: colony characterized by piling up and criss-cross pattern of growth) itself. This study was performed to examine the properties of these colonies. Secondary or tertiary cultures of SHE cells were treated with benzo [a] pyrene or N-methyl-N'-nitro-N-nitrosoguanidine. In total, 37 ETCs and 17 normal colonies (NCs) were cloned and analyzed. Obtained results were as follows: (1) Stability of transformed morphol.; immediately after cloning, the cells from 3/37 of the ETCs maintained their transformed phenotype, but all cells from other ETCs (34/37) showed flat or well-oriented morphol. Thus, the "transformed" morphol. of more than 90% of the ETCs was reversible. (2) Chromosome abnormality; 3/15 of the clones from ETCs were hypo diploid or tetraploid, while the others (12/15) were normal diploid immediately after cloning. (3) Immortalization; up to about one month after cloning, most of the clones (from transformed or normal colonies) could be subcultured at 1:2 or 1:4 split ratio per wk, but thereafter all the clones ceased growing. After about a one month or longer latency, 6/37 of the clones from ETCs and 4/17 of the clones from NCs restarted growing and acquired immortality. That is, there was no significant difference in the frequency of immortalization between ETCs and NCs. Thus, from the present expt., there was no direct evidence that ETC \*\*\*correlates\*\*\* to acquisition of immortality or tumorigenesis. Further expts. (e.g. comparison of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* between cells from

transformed and normal colonies using microarray) would be required to give a logical meaning to this short-term transformation \*\*\*assay\*\*\*  
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2004:140983 CAPLUS DN 140:214544

TI Gene array identification of osteoclast genes: Differential inhibition of osteoclastogenesis by cyclosporin A and granulocyte macrophage colony stimulating factor

AU Day, Christopher J.; Kim, Michael S.; Stephens, Sebastien R. J.; Simcock, Wendy E.; Aitken, Cathy J.; Nicholson, Geoff C.; Morrison, Nigel A.

CS School of Health Sciences, Griffith University, Southport, 4215, Australia

SO Journal of Cellular Biochemistry (2003), Volume Date 2004, 91(2), 303-315 CODEN: JCEBD5; ISSN: 0730-2312

PB Wiley-Liss, Inc.

DT Journal

LA English

AB Treatment of adherent peripheral blood mononuclear cells (PBMCs) with macrophage colony stimulating factor (M-CSF) and receptor activator of NF- $\kappa$ B ligand (RANKL) stimulates the formation of multinucleate osteoclast-like cells. Treatment with M-CSF alone results in the formation of macrophage-like cells. Through the use of Atlas human cDNA expression arrays, genes regulated by RANKL were identified. Genes include numerous cytokines and cytokine receptors (RANTES and CSF2R.infin.), transcription factors (nuclear factor of activated T-cells cytoplasmic 1 (NFATc1) and GA binding protein transcription factor alpha (GABP.alpha.)), and ribosomal proteins (60S L17 and 40S S20). Real-time PCR anal. showed significant \*\*\*correlation\*\*\* (R2 of 0.98 P < 0.01) with array data for all genes \*\*\*tested\*\*\*. Time courses showed differential activation patterns of transcription factors with early induction of FUSE binding protein 1 (FBP) and c-Jun, and later steady upregulation of NFATc1 and GABP by RANKL. Treatment with cyclosporin A, a known NFATc1 inhibitor, resulted in a blockade of osteoclast formation. The mononuclear cells resulting from high cyclosporin treatment (1,000 ng/mL) were cathepsin K (CTSK) and tartrate-resistant acid phosphatase (TRAP) pos. but expression of calcitonin receptor (CTR) was downregulated by more than 30-fold. Const. exposure of M-CSF- and RANKL-treated cells to GM-CSF resulted in inhibition of osteoclast formation and the downregulation of CTSK and TRAP implicating the upregulation of CSF2R in a possible feedback inhibition of osteoclastogenesis.

L9 ANSWER 8 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2004:34495 CAPLUS DN 140:247328

TI Similarities and differences in uterine \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\* caused by treatment with physiological and non-physiological estrogens

AU Watanabe, H.; Suzuki, A.; Kobayashi, M.; Lubahn, D. B.; Handa, H.; Iguchi, T.

CS Center for Integrative Bioscience, Okazaki National Research Institutes and Core Research for Evolution Science and Technology (CREST), Japan Science and Technology Corporation, Okazaki, 444-8585, Japan

SO Journal of Molecular Endocrinology (2003), 31(3), 487-497 CODEN: JMLEEI; ISSN: 0952-5041

PB Society for Endocrinology

DT Journal

LA English

AB Administration of physiol. and non-physiol. estrogens during pregnancy or after birth is known to have adverse effects on the development of the reproductive tract and other organs.

Although it is believed that both estrogens have similar effects on gene expression, this view has not been \*\*\*tested\*\*\*

systematically. To compare the effects of physiol. (estradiol; E2) and non-physiol. (diethylstilbestrol; DES) estrogens, we used DNA microarray anal. to examine the uterine \*\*\*gene\*\*\*

\*\*\*expression\*\*\* \*\*\*patterns\*\*\* induced by the two

estrogens. Although E2 and DES induced many genes to respond in the same way, different groups of genes showed varying levels

of maximal activities to each estrogen, resulting in different dose-response patterns. Thus, each estrogen has a distinct effect on

uterine gene expression. The genes were classified into clusters according to their dose-responses to the two estrogens. Of the

eight clusters, only two \*\*\*correlated\*\*\* well with the uterotrophic effect of different doses of E2. One of these clusters

contained genes that were upregulated by E2, which included genes encoding several stress proteins and transcription factors.

The other cluster contained genes that were downregulated by E2, including genes related to metab., transcription and

detoxification processes. The expression of these genes in estrogen receptor-deficient mice was not affected by E2

treatment, indicating that these genes are affected by the E2-bound estrogen receptor. Thus, of the many genes that are

affected by estrogen, it was suggested that only a small no. are directly involved in the uterotrophic effects of estrogen treatment.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2004:8212 CAPLUS DN 140:162143

TI Microarray analysis of tumor necrosis factor .alpha. induced gene expression in U373 human glioblastoma cells

AU Schwamborn, Jens; Lindecke, Antje; Elvers, Margitta; Horejschi, Volker; Kerick, Martin; Rafigh, Mehran; Pfeiffer, Julia; Pruellage, Maria; Kaltschmidt, Barbara; Kaltschmidt, Christian

CS Institute of Neurobiochemistry, University of Witten/Herdecke, Witten, D-58448, Germany

SO BMC Genomics (2003), 4, No pp. given CODEN: BGMEET; ISSN: 1471-2164 URL: <http://www.biomedcentral.com/1471-2164/4/46>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Tumor necrosis factor .alpha. (TNF) is able to induce a variety of biol. responses in the nervous system including

inflammation and neuroprotection. Human astrocytoma cells U373 have been widely used as a model for inflammatory

cytokine actions in the nervous system. Here the authors used cDNA microarrays to analyze the time course of the

transcriptional response from 1 h up to 12 h post TNF treatment in comparison to untreated U373 cells. TNF activated strongly

the NF- $\kappa$ B transcriptional pathway and is linked to other pathways via the NF- $\kappa$ B target genes JUNB and IRF-1. Part

of the TNF-induced gene expression could be inhibited by pharmacol. inhibition of NF- $\kappa$ B with pyrrolidine-

dithiocarbamate (PDTTC). NF- $\kappa$ B comprises a family of transcription factors which are involved in the inducible

expression of genes regulating neuronal survival, inflammatory response, cancer, and innate immunity. Here, the authors show

that numerous genes responded to TNF (>880 from 7500

\*\*\*tested\*\*\* ) with a >2-fold induction rate. Several novel TNF-responsive genes (about 60% of the genes regulated by a factor .gtoreq.3) were detected. A comparison of the authors' TNF-induced \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of U373, with \*\*\*profiles\*\*\* from 3T3 and Hela cells revealed a striking cell-type specificity. SCYA2 (MCP-1, CCL2, MCAF) was induced in U373 cells in a sustained manner and at the highest level of all analyzed genes. MCP-1 protein expression, as monitored with immunofluorescence and ELISA, \*\*\*correlated\*\*\* exactly with microarray data. Based on these data and on evidence from literature the authors suggest a model for the potential neurodegenerative effect of NF- $\kappa$ B in astroglia: Activation of NF- $\kappa$ B via TNF results in a strongly increased prodn. of MCP-1. This leads to an exacerbation of neurodegeneration in stroke or multiple sclerosis, presumably via infiltration of macrophages. Thus, the vast majority of genes regulated >3-fold were previously not linked to tumor necrosis factor .alpha. as a search in published literature revealed. Striking co-regulation for several functional groups such as proteasome and ribosomal proteins were detected.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:1009767 CAPLUS  
DN 140:109215  
TI Identification of Genes Expressed in Malignant Cells that Promote Invasion  
AU Walter-Yohrling, Jennifer; Cao, Xiaohong; Callahan, Michele; Weber, William; Morgenbesser, Sharon; Madden, Stephen L.; Wang, Clarence; Teicher, Beverly A.  
CS Genzyme Corporation, Framingham, MA, 01701-9322, USA  
SO Cancer Research (2003), 63(24), 8939-8947 CODEN: CNREA8; ISSN: 0008-5472  
PB American Association for Cancer Research  
DT Journal  
LA English  
AB To systematically identify genes related to invasion a three-dimensional multicellular matrix invasion \*\*\*assay\*\*\* was used to classify human tumor cell lines as stromal invasion pos. or stromal invasion neg. Cells from two of the primary cell types of the stromal compartment [endothelial cells (HMVEC) and myofibroblasts (HDF)] were \*\*\*assayed\*\*\* for invasion into tumor cell clusters (breast carcinoma, ovarian carcinoma, prostate carcinoma, lung carcinoma, and melanoma). Four tumor cell lines (MDA-MB231, SKOV-3, A375, and MEL624) scored invasion pos., and four tumor cell lines (LNCaP, DU145, PC3, and A549) scored invasion neg. Serial anal. of gene expression (SAGE) libraries generated from the tumor cell lines were analyzed by GeneSpring Hierarchical clustering, t \*\*\*test\*\*\*, and .chi.2 \*\*\*test\*\*\*. Clusters emerged that reflected the behavior in the cell culture \*\*\*assay\*\*\*. Of the 47 most highly differentially expressed genes, 30 were selected for confirmation by real-time PCR, and 9 had good \*\*\*correlation\*\*\* with normalized serial anal. of gene expression tag counts. The strongest \*\*\*correlations\*\*\* were for bone marrow stromal antigen 2, stathmin-like 3, tumor necrosis factor receptor superfamily member 5, and hepatocyte growth factor tyrosine kinase substrate. In situ hybridization of metastatic and nonmetastatic ovarian cancer demonstrated selective expression of bone marrow stromal antigen 2 and tumor necrosis factor receptor superfamily member 5 in the metastatic disease. This combination approach appears to be a powerful tool for identifying genes that may be useful as diagnostic markers and/or as therapeutic targets for invasive solid tumors.

RE.CNT 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:980085 CAPLUS  
DN 140:123340  
TI Normality of oligonucleotide microarray data and implications for parametric statistical analyses  
AU Giles, Peter J.; Kipling, David  
CS Department of Pathology, University of Wales College of Medicine, Cardiff, CF14 4XN, UK  
SO Bioinformatics (2003), 19(17), 2254-2262 CODEN: BOINFP; ISSN: 1367-4803  
PB Oxford University Press  
DT Journal  
LA English  
AB Exptl. limitations have resulted in the popularity of parametric statistical \*\*\*tests\*\*\* as a method for identifying differentially regulated genes in microarray data sets. However, these \*\*\*tests\*\*\* assume that the data follow a normal distribution. To date, the assumption that replicate expression values for any gene are normally distributed, has not been critically addressed for Affymetrix GeneChip data. The normality of the expression values calcd. using four different com. and academic software packages was investigated using a data set consisting of the same target RNA applied to 59 human Affymetrix U95A GeneChips using a combination of statistical \*\*\*tests\*\*\* and visualization techniques. For the majority of probe sets obtained from each anal. suite, the expression data showed a good \*\*\*correlation\*\*\* with normality. The exception was a large no. of low-expressed genes in the data set produced using Affymetrix Microarray Suite 5.0, which showed a striking non-normal distribution. In summary, our data provide strong support for the application of parametric \*\*\*tests\*\*\* to GeneChip data sets without the need for data transformation.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:967515 CAPLUS  
DN 140:251163  
TI Osteopontin identified as colon cancer tumor progression marker  
AU Agrawal, Deepak; Chen, Tingan; Irby, Rosalyn; Quackenbush, John; Chambers, Ann F.; Szabo, Marianna; Cantor, Alan; Coppola, Domenico; Yeatman, Timothy J.  
CS H. Lee Moffitt Cancer Center, Department of Cell Biology, University of South Florida, Tampa, FL, USA  
SO Comptes Rendus Biologies (2003), 326(10-11), 1041-1043 CODEN: CRBOCM; ISSN: 1631-0691  
PB Editions Scientifiques et Medicales Elsevier  
DT Journal  
LA English  
AB Identifying mol. markers for colon cancer is a top priority. Using a pooled sample approach with Affymetrix GeneChip technol., we \*\*\*assayed\*\*\* colon cancers derived from a series of clin. stages to identify mol. markers of potential prognostic value. Of 12,000 genes assessed, osteopontin emerged as the leading candidate tumor progression marker. Osteopontin is a secreted glycoprotein known to bind integrins and CD44. Its actual mol. function remains elusive but its increased expression \*\*\*correlates\*\*\* strongly with tumor progression.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR  
THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 13 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:952785 CAPLUS  
DN 140:125473

TI Pheromone-mediated gene expression in the honey bee brain  
AU Grozinger, Christina M.; Sharabash, Noura M.; Whitfield,  
Charles W.; Robinson, Gene E.

CS Beckman Institute for Advanced Science and Technology,  
University of Illinois at Urbana-Champaign, Urbana, IL, 61801,  
USA

SO Proceedings of the National Academy of Sciences of the  
United States of America (2003), 100(Suppl. 2), 14519-14525  
CODEN: PNAS6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB We \*\*\*tested\*\*\* the hypothesis that queen mandibular  
pheromone (QMP) causes changes in gene expression in the  
brain of the adult worker honey bee, and that these changes can  
be \*\*\*correlated\*\*\* to the downstream behavioral responses  
induced by QMP. In support of the 1st hypothesis, cage expts.  
revealed that QMP transiently regulated expression of several  
hundred genes and chronically regulated the expression of 19  
genes. Several of these genes were also affected by QMP in  
expts. with bee colonies in the field, demonstrating robust gene  
regulation by pheromone. To evaluate the 2nd hypothesis, we  
focused on 1 function of QMP: delaying the transition from  
working in the hive (e.g., brood care, or nursing) to foraging.  
We compared the list of QMP-regulated genes with the lists of  
genes differentially regulated in nurse and forager brains  
generated in a sep. study. QMP consistently activated nursing  
genes and repressed foraging genes, suggesting that QMP may  
delay behavioral maturation by regulating genes in the brain that  
produce these behavioral states. We also report here on an  
ortholog of the Drosophila transcription factor kruppel homolog 1  
that was strongly regulated by QMP, esp. in the mushroom  
bodies of the bee brain. These results demonstrate chronic gene  
regulation by a primer pheromone and illustrate the potential of  
genomics to trace the actions of a pheromone from perception to  
action, and thereby provide insights into how pheromones  
regulate social life.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 14 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:943097 CAPLUS  
DN 141:33402

TI Paclitaxel and cisplatin-induced neurotoxicity: a protective  
role of acetyl-L-carnitine

AU Pisano, Claudio; Pratesi, Graziella; Laccabue, Diletta; Zunino,  
Franco; Lo Giudice, Pietro; Bellucci, Augusta; Pacifici, Licia;  
Camerini, Barbara; Vesci, Loredana; Castorina, Massimo; Cicuzza,  
Sandra; Tredici, Giovanni; Marmiroli, Paola; Nicolini, Gabriella;  
Galbiati, Stefania; Calvani, Menotti; Carminati, Paolo; Cavaletti,  
Guido

CS Research and Development, Sigma-Tau S.p.A. Industrie  
Farmaceutiche Riunite, Rome, Italy

SO Clinical Cancer Research (2003), 9(15), 5756-5767 CODEN:  
CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB Antineoplastic drugs belonging to platinum or taxane  
families are severely neurotoxic, inducing the onset of disabling  
peripheral neuropathies with different clin. signs. Acetyl-L-  
carnitine (ALC) is a natural occurring compd. with a  
neuroprotective activity in several exptl. paradigms. In this study  
we have \*\*\*tested\*\*\* the hypothesis that ALC may have a  
protective role on cisplatin and paclitaxel-induced neuropathy.  
Sensory nerve conduction velocity (SNCV) was measured in rats  
before, at end, and after an addnl. follow-up period from  
treatments with cisplatin, paclitaxel, or with the resp.  
combination with ALC. In addn., serum from treated animals was  
collected to measure the levels of circulating NGF, and left sciatic  
nerves were processed for light and electron microscope  
observations. ALC interference on cisplatin and paclitaxel  
antitumor activity and protective mechanisms were investigated  
using several in vitro and in vivo models. ALC co-treatment was  
able to significantly reduce the neurotoxicity of both cisplatin and  
paclitaxel in rat models, and this effect was \*\*\*correlated\*\*\*  
with a modulation of the plasma levels of NGF in the cisplatin-  
treated animals. Moreover, expts. in different tumor systems  
indicated the lack of interference of ALC in the antitumor effects  
of cisplatin and paclitaxel. The transcriptional \*\*\*profile\*\*\* of  
\*\*\*gene\*\*\* \*\*\*expression\*\*\* in PC12 cells indicated that  
ALC, in the presence of NGF, was able to pos. modulate NGFI-A  
expression, a gene relevant in the rescue from tissue-specific  
toxicity. Finally, the transcriptionally ALC-mediated effects were  
\*\*\*correlated\*\*\* to increase histone acetylation. In conclusion,  
our results indicate that ALC is a specific protective agent for  
chemotherapy-induced neuropathy after cisplatin or paclitaxel  
treatment without showing any interference with the antitumor  
activity of the drugs.

RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 15 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:943080 CAPLUS  
DN 140:179142

TI Clinical screening of gene rearrangements in childhood  
leukemia by using a multiplex polymerase chain reaction-  
microarray approach

AU Nasedkina, Tatyana V.; Zharinov, Vladislav S.; Isaeva,  
Ekaterina A.; Mityaeva, Olga N.; Yurasov, Roman N.; Surzhikov,  
Sergei A.; Turgin, Alexander Y.; Rubina, Alla Y.; Karachunskii,  
Alexander I.; Gartenhaus, Ronald B.; Mirzabekov, Andrei D.

CS Engelhardt Institute of Molecular Biology, Russian Academy  
of Sciences, Moscow, Russia

SO Clinical Cancer Research (2003), 9(15), 5620-5629 CODEN:  
CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB Currently, many forms of leukemia are considered potentially  
curable, with prognosis and clin. outcome strongly dependent on  
the underlying mol. pathophysiol. A substantial no. of leukemia  
patients harbor nonrandom karyotypic abnormalities that define  
subgroups with unique biol. and clin. features. For detection of  
these types of gene rearrangements, a combination of multiplex  
RT-PCR with hybridization on oligonucleotide gel array was  
presented previously, which identified five chromosomal  
translocations with fusion variants. In the present study, addnl.  
clin. relevant translocations were included in the anal. using a  
second generation of microarrays. The authors also expanded  
significantly on the clin. \*\*\*correlation\*\*\* of our findings. An  
oligonucleotide microarray was designed for hybridization with  
products of a multiplex RT-PCR to identify the following



translocations: t(9;22)p190, t(4;11), t(12;21), t(1;19), typical for acute lymphoblastic leukemia; t(9;22)p210 for chronic myeloid leukemia; and t(8;21), t(15;17), inv16, typical for acute myeloblastic leukemia. To demonstrate the potential clin. application of the method, 247 cases of childhood leukemia were screened, and the above-mentioned gene rearrangements were found in 30% of cases. The sensitivity and specificity of the \*\*\*assay\*\*\* is comparable with the RT-PCR technique, so that it can be used to follow minimal residual disease. The feasibility of an addnl. refinement of the method, on-chip-multiplex PCR, has been successfully demonstrated by identifying a common translocation, t(9;22), in chronic myeloid leukemia. These data suggest that the microarray-based \*\*\*assay\*\*\* can be an effective and reliable tool in the clin. screening of leukemia patients for the presence of specific gene rearrangements with important diagnostic and prognostic implications. The method is amenable for automation and high-throughput anal.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:942767 CAPLUS DN 140:40262

TI Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics

IN Nevins, Joseph; West, Mike; Goldschmidt, Pascal

PA Duke University, USA

SO PCT Int. Appl., 408 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI WO 2003091391 A2 20031106 WO 2002-XB38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG WO 2003091391 A2 20031106 WO 2002-US38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRAI US 2002-374547P P 20020423 US 2002-420784P P 20021024 US 2002-421043P P 20021025 US 2002-424680P P 20021108 WO 2002-US38221 A 20021112

AB Genes whose expression is correlated with an determinant of an atherosclerotic phenotype are provided. Also provided are methods of using the subject atherosclerotic determinant genes in diagnosis and treatment methods, as well as drug screening methods. In addn., reagents and kits thereof that find use in practicing the subject methods are provided. Also provided are methods of detg. whether a gene is correlated with a disease

phenotype, where correlation is detd. using a Bayesian anal. [This abstr. record is one of three records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 17 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:942764 CAPLUS

DN 140:3792

TI Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics

IN Nevins, Joseph; West, Mike; Goldschmidt, Pascal

PA Duke University, USA

SO PCT Int. Appl., 408 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI WO 2003091391 A2 20031106 WO 2002-XA38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG WO 2003091391 A2 20031106 WO 2002-US38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG PRAI US 2002-374547P P 20020423 US 2002-420784P P 20021024 US 2002-421043P P 20021025 US 2002-424680P P 20021108 WO 2002-US38221 A 20021112

AB Genes whose expression is correlated with an determinant of an atherosclerotic phenotype are provided. Also provided are methods of using the subject atherosclerotic determinant genes in diagnosis and treatment methods, as well as drug screening methods. In addn., reagents and kits thereof that find use in practicing the subject methods are provided. Also provided are methods of detg. whether a gene is correlated with a disease phenotype, where correlation is detd. using a Bayesian anal.

L9 ANSWER 18 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:937673 CAPLUS DN 140:109698

TI Quantitative cytokine gene expression in human tonsils at excision and during histoculture assessed by standardized and calibrated real-time PCR and novel data processing

AU Bonanomi, Athos; Kojic, Dejan; Giger, Bettina; Rickenbach, Zaira; Jean-Richard-Dit-Bressel, Louis; Berger, Christoph; Niggli, Felix K.; Nadal, David

CS Divisions of Infectious Diseases and Oncology, Functional Genomics Unit, University Children's Hospital of Zurich, Zurich, Switz.

SO Journal of Immunological Methods (2003), 283(1-2), 27-43 CODEN: JIMMBG; ISSN: 0022-1759

PB Elsevier B.V.  
DT Journal  
LA English

AB Real-time reverse transcription polymerase chain reaction (RT-PCR) **\*\*\*assays\*\*\*** were developed for the quantification of expression of the genes for human interleukin (IL)-1 $\beta$ , IL-2, IL-6, IL-8, IL-10, IL-12, IL-15, interferon (IFN)- $\gamma$ , tumor necrosis factor (TNF)- $\alpha$ , transforming growth factor (TGF)- $\beta$ , and for the endogenous ref. hydroxymethylbilane synthase (HMBS). The **\*\*\*assays\*\*\*** detected as little as five plasmid copies and were 100% specific. The creation and integration of a calibration sample into the **\*\*\*assays\*\*\*** permitted their calibration across expts. To handle the high no. of generated data, the **\*\*\*correlator\*\*\*** of advanced real-time **\*\*\*assays\*\*\*** (CARTA) software was designed to organize samples and to automatically control and analyze TaqMan real-time RT-PCR data. The RT-PCR **\*\*\*assays\*\*\*** were applied to quantify levels of cytokine gene expression in human palatine tonsils at excision and during 4 days of histoculture. Similar longitudinal **\*\*\*patterns\*\*\*** of cytokine **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** were obsd. in all donors, but the variations in spontaneous expression levels between donors were large. The expression levels in histocultures were const. over time and similar to the expression levels at excision except for IL-6 and IL-8, which markedly increased following the first 24 h of culture, possibly due to the initial stress. The standardized and calibrated RT-PCR **\*\*\*assays\*\*\*** quantify gene expression of human cytokines proved sensitive and specific for the investigation of cell behavior at the mol. level and the newly established CARTA software, a reliable tool for rapid data handling. Tonsil histocultures could serve as a valuable ex vivo model system for further, donor-dependent, studies on activation or repression of cytokine gene expression.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:915162 CAPLUS  
DN 140:56494

TI What affects mRNA levels in leaves of field-grown aspen? A study of developmental and environmental influences

AU Wissel, Kirsten; Pettersson, Fredrik; Berglund, Anders; Jansson, Stefan

CS Umea Plant Science Centre, Department of Plant Physiology, University of Umea, Umea, S-901 87, Swed.

SO Plant Physiology (2003), 133(3), 1190-1197 CODEN: PLPHAY; ISSN: 0032-0889

PB American Society of Plant Biologists

DT Journal

LA English

AB We have analyzed the abundance of mRNAs expressed from 11 nuclear genes in leaves of a free-growing aspen (*Populus tremula*) tree throughout the growing season. We used multivariate statistics to det. the influence of environmental factors (i.e. the weather before sampling) and developmental responses to seasonal changes at the mRNA level for each of these genes. The gene encoding a germin-like protein was only expressed early in the season, whereas the other **\*\*\*tested\*\*\*** genes were expressed throughout the season and showed mRNA variations on a day-to-day basis. For six of the genes, reliable models were found that described the mRNA level as a function of weather, but the leaf age was also important for all genes except one encoding an early light-inducible protein (which appeared to be regulated purely by environmental factors under these conditions). The results confirmed the importance of

several environmental factors previously shown to regulate the genes, but we also detected a no. of less obvious factors (such as the variation in weather parameters and the weather of the previous day) that **\*\*\*correlated\*\*\*** with the mRNA levels of individual genes. The study shows the power of multivariate statistical methods in analyzing gene regulation under field conditions.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:891667 CAPLUS  
DN 140:36473

TI Gene expression phenotypes of oncogenic signaling pathways

AU Huang, Erich S.; Black, Esther P.; Dressman, Holly; West, Mike; Nevins, Joseph R.

CS Department of Molecular Genetics and Microbiology; Duke University Medical Center, Duke University, Durham, NC, USA

SO Cell Cycle (2003), 2(5), 415-417 CODEN: CCEYAS; ISSN: 1538-4101

PB Landes Bioscience

DT Journal; General Review

LA English

AB A review on the application of gene expression technol. to the study of oncogenic signaling pathways. The power of gene expression anal. was used to uncover greater detail in these pathways and to define "signatures" of the activation of the oncogenic pathways that could then be applied to the study of tumor development. The process began with the use of a controlled exptl. system for inducing activities known to be involved in proliferation and oncogenesis in mouse embryo fibroblasts. Gene expression information was collected subsequently from these cells, identifying structure in these data. Using robust statistical procedures to **\*\*\*correlate\*\*\*** data structure, termed "metagenes", with the state of pathway deregulation within the cells, **\*\*\*testable\*\*\*** models were developed from these exptl. data.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:888924 CAPLUS  
DN 140:71738

TI Probabilistic estimation of micro-array data reliability and underlying gene expression

AU Bilke, Sven; Breslin, Thomas; Sigvardsson, Mikael

CS Complex Systems Division, Department of Theoretical Physics, University Of Lund, Lund, SE-223 62, Swed.

SO BMC Bioinformatics (2003), 4, No pp. given CODEN: BBMIC4; ISSN: 1471-2105 URL:

<http://www.biomedcentral.com/1471-2105/4/40>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB The availability of high throughput methods for measurement of mRNA concns. makes the reliability of conclusions drawn from the data and global quality control of samples and hybridization important issues. We address these issues by an information theoretic approach, applied to discretized expression values in replicated gene expression data. The approach yields a quant. measure of two important parameter classes: First, the probability  $P(\sigma_i | S)$  that a gene is in the biol. state  $\sigma_i$  in a certain variety, given its obsd.

expression S in the samples of that variety. Second, sample specific error probabilities which serve as consistency indicators of the measured samples of each variety. The method and its limitations are \*\*\*tested\*\*\* on gene expression data for developing murine B-cells and a t- \*\*\*test\*\*\* is used as ref. On a set of known genes it performs better than the t- \*\*\*test\*\*\* despite the crude discretization into only two expression levels. The consistency indicators, i.e. the error probabilities, \*\*\*correlate\*\*\* well with variations in the biol. material and thus prove efficient. The proposed method is effective in detg. differential gene expression and sample reliability in replicated microarray data. Already at two discrete expression levels in each sample, it gives a good explanation of the data and is comparable to std. techniques.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:885931 CAPLUS DN 139:362709

TI Activation of NF- $\kappa$ B by Toxoplasma gondii \*\*\*correlates\*\*\* with increased expression of antiapoptotic genes and localization of phosphorylated I. $\kappa$ B to the parasitophorous vacuole membrane  
AU Molestina, Robert E.; Payne, T. Matthew; Coppens, Isabelle; Sinai, Anthony P.

CS Department of Microbiology, Immunology, and Molecular-Genetics, University of Kentucky College of Medicine, Lexington, KY, 40536, USA  
SO Journal of Cell Science (2003), 116(21), 4359-4371 CODEN: JNCSAI; ISSN: 0021-9533

PB Company of Biologists Ltd.  
DT Journal  
LA English

AB Mammalian cells infected with Toxoplasma gondii are resistant to apoptosis induced by a variety of stimuli. We have demonstrated that the host transcription factor NF- $\kappa$ B plays a pivotal role in the T.-gondii-mediated blockade of apoptosis because inhibition is lost in cells lacking the p65 (RelA) subunit of NF- $\kappa$ B (p65-/-). In the present study, we examd. the effects of T. gondii infection on NF- $\kappa$ B activation and the expression of genes involved in the apoptotic cascade. Infection of wild-type mouse embryonic fibroblasts (MEFs) with T.-gondii-induced nuclear translocation of the p50 and p65 subunits of NF- $\kappa$ B as examd. by immunoblotting of nuclear exts., immunofluorescence and electrophoretic mobility shift \*\*\*assays\*\*\*. A comparison of apoptotic \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* from wild-type and p65-/- MEFs revealed distinct patterns of induction in response to T. gondii infection. In particular, the differences seen in the Bcl-2 and IAP families are consistent with the antiapoptotic responses obsd. in the resistant wild-type cells compared with the sensitive p65-/- fibroblasts. Consistent with NF- $\kappa$ B activation, T. gondii infection promoted phosphorylation of the inhibitor I. $\kappa$ B. Interestingly, phosphorylated I. $\kappa$ B was concd. on the parasitophorous vacuole membrane (PVM), suggesting a parasite-directed event. Results from this study suggest that activation of NF- $\kappa$ B plays an important role in stimulation of antiapoptotic gene expression by T. gondii. Furthermore, recruitment of phosphorylated I. $\kappa$ B to the PVM implies the presence of intrinsic factor(s) in T. gondii that might be used to manipulate the NF- $\kappa$ B signaling pathway in the host to elicit a survival response during infection.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:883707 CAPLUS DN 140:26254

TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* of normal lungs predicts genetic predisposition to lung cancer in mice

AU Gariboldi, Manuela; Spinola, Monica; Milani, Silvano; Pignatiello, Carmen; Kadota, Koji; Bono, Hidemasa; Hayashizaki, Yoshihide; Dragani, Tommaso A.; Okazaki, Yasushi

CS Department of Experimental Oncology, Istituto Nazionale Tumori, Milan, Italy

SO Carcinogenesis (2003), 24(11), 1819-1826 CODEN: CRNGDP; ISSN: 0143-3334

PB Oxford University Press

DT Journal

LA English

AB Genetic susceptibility to lung tumorigenesis shows large variations among mouse strains. To \*\*\*test\*\*\* whether genetic predisposition to lung tumorigenesis is assocd. with a specific \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* in normal lungs, the authors analyzed gene expression in 16 inbred strains of known susceptibility/resistance to lung tumorigenesis, using the RIKEN mouse full-length cDNA 19K microarray set. The strain-specific \*\*\*expression\*\*\* \*\*\*profile\*\*\* of 91 cDNA clones \*\*\*correlated\*\*\* with strain lung tumor susceptibility/resistance and predicted, by principal component anal., the genetic predisposition to lung tumorigenesis in mice.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:879089 CAPLUS DN 140:3220

TI Absolute \*\*\*Gene\*\*\* \*\*\*Expression\*\*\*

\*\*\*Patterns\*\*\* of Thioredoxin and Glutaredoxin Redox Systems in Mouse

AU Jurado, Juan; Prieto-Alamo, Maria-Jose; Madrid-Risquez, Jose; Pueyo, Carmen

CS Departamento de Bioquímica y Biología Molecular, Universidad de Córdoba, Córdoba, 14071, Spain

SO Journal of Biological Chemistry (2003), 278(46), 45546-45554 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB This work provides the first abs. expression patterns of genes coding for all known components of both thioredoxin (Trx) and glutaredoxin (Grx) systems in mouse: Trx1, Trx2, Grx1, Grx2, TrxR1, TrxR2, thioredoxin/glutathione reductase, and glutathione reductase. We devised a novel \*\*\*assay\*\*\* that, combining the advantages of multiplex and real-time PCR, streamlines the quantitation of the actual mRNA copy nos. in whole-animal expts. Quantitations reported establish differences among adult organs and embryonic stages, compare mRNA decay rates, explore the significance of alternative mRNA isoforms derived from TrxR1 and Grx2 genes, and examine the time-course expression upon superoxide stress promoted by paraquat. Collectively, these quantitations show: (i) unique \*\*\*expression\*\*\* \*\*\*profiles\*\*\* for each transcript and mouse organ examd., yet with some general trends like the higher amts. of mRNA species coding for thioredoxins than those

coding for the reductases that control their redox states and activities; (ii) continuous expression during embryogenesis with outstanding up-regulations of Trx1 and TrxR1 mRNAs in specific temporal sequences; (iii) drastic differences in mRNA stability, liver decay rates range from 2.8 h (thioredoxin/glutathione reductase) to .gtoreq.=" BORDER="0".degree. 35 h (Trx1 and Trx2), and directly \*\*\*correlate\*\*\* with mRNA steady-state values; (iv) \*\*\*testis\*\*\* -specific differences in the amts. (relative to total isoforms) of transcripts yielding the mitochondrial Grx2a and 67-kDa TrxR1 variants; and (v) coordinated up-regulation of TrxR1 and glutathione reductase mRNAs in response to superoxide stress in an organ-specific manner. Further insights into in vivo roles of these redox systems should be gained from more focused studies of the mechanisms underlying the vast differences reported here at the transcript level.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:878825 CAPLUS DN 140:54107

TI Normalization of DNA-microarray data by nonlinear \*\*\*correlation\*\*\* maximization

AU Faller, D.; Voss, H. U.; Timmer, J.; Hobohm, U. CS Freiburg Center for Data Analysis and Modelin, Freiburg, 79104, Germany

SO Journal of Computational Biology (2003), 10(5), 751-762 CODEN: JCOBEM; ISSN: 1066-5277

PB Mary Ann Liebert, Inc.

DT Journal

LA English

AB Signal data from DNA-microarray ("chip") technol. can be noisy; i.e., the signal variation of one gene on a series of repetitive chips can be substantial. It is becoming more and more recognized that a sufficient no. of chip replicates has to be made in order to sep. correct from incorrect signals. To reduce the systematic fraction of the noise deriving from pipetting errors, from different treatment of chips during hybridization, and from chip-to-chip manufg. variability, normalization schemes are employed. We present here an iterative nonparametric nonlinear normalization scheme called simultaneous alternating conditional expectation (SACE), which is designed to maximize \*\*\*correlation\*\*\* between chip repeats in all-chip-against-all space. We \*\*\*tested\*\*\* SACE on 28 expts. with 158 Affymetrix one-color chips. The procedure should be equally applicable to other DNA-microarray technologies, e.g., two-color chips. We show that the redn. of noise compared to a simple normalization scheme like the widely used linear global normalization leads to fewer false-pos. calls, i.e., to fewer genes which have to be laboriously confirmed by independent methods such as TaqMan or quant. PCR.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:875393 CAPLUS DN 139:363045

TI Genes expressed in atherosclerotic tissue and their use in diagnosis and pharmacogenetics

IN Nevins, Joseph; West, Mike; Goldschmidt, Pascal

PA Duke University, USA

SO PCT Int. Appl., 408 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3 PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2003091391 A2 20031106 WO 2002-US38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG WO 2003091391 A2 20031106 WO 2002-XA38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG WO 2003091391 A2 20031106 WO 2002-XB38221 20021112 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2003224383 A1 20031204 US 2002-291885 20021112 PRAI US 2002-374547P P 20020423 US 2002-420784P P 20021024 US 2002-421043P P 20021025 US 2002-424680P P 20021108 WO 2002-US38221 A 20021112

AB Genes whose expression is correlated with an determinant of an atherosclerotic phenotype are provided. Also provided are methods of using the subject atherosclerotic determinant genes in diagnosis and treatment methods, as well as drug screening methods. In addn., reagents and kits thereof that find use in practicing the subject methods are provided. Also provided are methods of detg. whether a gene is correlated with a disease phenotype, where correlation is detd. using a Bayesian anal.

L9 ANSWER 27 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:874013 CAPLUS DN 140:192431

TI Identification of common or distinct genes related to antitumor activities of a medicinal herb and its major component by oligonucleotide microarray

AU Iizuka, Norio; Oka, Masaaki; Yamamoto, Kotaro; Tangoku, Akira; Miyamoto, Koji; Miyamoto, Takanobu; Uchimura, Shunji; Hamamoto, Yoshihiko; Okita, Kiwamu

CS Department of Bioregulatory Function, Yamaguchi University School of Medicine, Yamaguchi, Japan

SO International Journal of Cancer (2003), 107(4), 666-672

CODEN: IJCNW; ISSN: 0020-7136

PB Wiley-Liss, Inc.

DT Journal

LA English

AB Although the physiol. actions of many herbs are gradually being elucidated at the mol. level, it remains unclear how individual components of herbs contribute to their biol. activities. In the present study, the antiproliferative activity of Coptidis rhizoma, a medicinal herb, and the major component berberine was investigated in 8 human pancreatic cancer cell lines.

\*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\* assocd. with sensitivities to each agent were analyzed with oligonucleotide arrays that comprised approx. 11,000 genes. We used a tetrazolium dye (MTT) \*\*\*assay\*\*\* to det. ID50 values after the 8 cell lines were exposed to the 2 agents for 72 h. The ID50 value for berberine was \*\*\*correlated\*\*\* pos. with that for C. rhizoma ( $r=0.725$ ,  $p=0.0401$ ). C. rhizoma killed tumor cells more effectively than purified berberine when normalized to the level of berberine present in the herb. From the oligonucleotide array data, we selected 20 and 13 genes with strong \*\*\*correlations\*\*\* ( $r_2 > 0.81$ ) to ID50 values for berberine and C. rhizoma, resp. Among these 33 genes, the levels of expression of 12 were \*\*\*correlated\*\*\* with the ID50 values of both agents, suggesting that these genes are assocd. with tumor-killing activity of berberine in C. rhizoma. Expression of the remaining 21 genes was \*\*\*correlated\*\*\* with the ID50 value of either purified berberine or C. rhizoma. Thus, we identified common and distinct genes responsible for anti-proliferative activities of purified berberine and C. rhizoma. This strategy may improve our understanding of the actions of herbs with antitumor activities.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:845012 CAPLUS DN 140:91599

TI A Training- \*\*\*Testing\*\*\* Approach to the Molecular Classification of Resected Non-Small Cell Lung Cancer  
AU Yamagata, Noboru; Shyr, Yu; Yanagisawa, Kiyoshi; Edgerton, Mary; Dang, Thao P.; Gonzalez, Adriana; Nadaf, Sorena; Larsen, Paul; Roberts, John R.; Nesbitt, Jonathan C.; Jensen, Roy; Levy, Shawn; Moore, Jason H.; Minna, John D.; Carbone, David P.  
CS Vanderbilt-Ingram Cancer Center and Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN, 37232-6838, USA  
SO Clinical Cancer Research (2003), 9(13), 4695-4704 CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research  
DT Journal  
LA English

AB RNA expression patterns assocd. with non-small cell lung cancer subclassification have been reported, but there are substantial differences in the key genes and clin. features of these subsets casting doubt on their biol. significance. In this study, the authors used a training- \*\*\*testing\*\*\* approach to \*\*\*test\*\*\* the reliability of cDNA microarray-based classifications of resected human non-small cell lung cancers (NSCLCs) analyzed by cDNA microarray. Groups of genes were identified that were able to differentiate primary tumors from normal lung and lung metastases, as well as identify known histol. subgroups of NSCLCs. Groups of genes were identified to discriminate sample clusters. A blinded confirmatory set of tumors was correctly classified by using these patterns. Some histol. diagnosed large cell tumors were clearly classified by \*\*\*expression\*\*\* \*\*\*profile\*\*\* anal. as being either adenocarcinoma or squamous cell carcinoma, indicating that this group of tumors may not be genetically homogeneous. High

.alpha.-actinin-4 expression was identified as highly \*\*\*correlated\*\*\* with poor prognosis. These results demonstrate that \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* can identify mol. classes of resected NSCLCs that correctly classifies a blinded \*\*\*test\*\*\* cohort, and \*\*\*correlates\*\*\* with and supplements std. histol. evaluation.  
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 29 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:824827 CAPLUS DN 140:36941

TI Prediction of regulatory networks: genome-wide identification of transcription factor targets from gene expression data  
AU Qian, Jiang; Lin, Jimmy; Luscombe, Nicholas M.; Yu, Haiyuan; Gerstein, Mark  
CS Department of Ophthalmology, Johns Hopkins Medical School, Baltimore, MD, 21287, USA  
SO Bioinformatics (2003), 19(15), 1917-1926 CODEN: BOINFP; ISSN: 1367-4803  
PB Oxford University Press  
DT Journal  
LA English

AB Defining regulatory networks, linking transcription factors (TFs) to their targets, is a central problem in post-genomic biol. One might imagine one could readily det. these networks through inspection of gene expression data. However, the relationship between the expression time course of a transcription factor and its target is not obvious (e.g. simple \*\*\*correlation\*\*\* over the time course), and current anal. methods, such as hierarchical clustering, have not been very successful in deciphering them. Here we introduce an approach based on support vector machines (SVMs) to predict the targets of a transcription factor by identifying subtle relationships between their \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. In particular, we used SVMs to predict the regulatory targets for 36 transcription factors in the Saccharomyces cerevisiae genome based on the microarray expression data from many different physiol. conditions. We trained and \*\*\*tested\*\*\* our SVM on a data set constructed to include a significant no. of both pos. and neg. examples, directly addressing data imbalance issues. This was non-trivial given that most of the known exptl. information is only for positives. Overall, we found that 63% of our TF-target relationships were confirmed through cross-validation. We further assessed the performance of our regulatory network identifications by comparing them with the results from two recent genome-wide ChIP-chip expts. Overall, we find the agreement between our results and these expts. is comparable to the agreement (albeit low) between the two expts. We find that this network has a delocalized structure with respect to chromosomal positioning, with a given transcription factor having targets spread fairly uniformly across the genome.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:817474 CAPLUS DN 140:192842

TI Transcriptome fingerprints distinguish hallucinogenic and nonhallucinogenic 5-hydroxytryptamine 2A receptor agonist effects in mouse somatosensory cortex  
AU Gonzalez-Maeso, Javier; Yuen, Tony; Ebersole, Barbara J.; Wurmbach, Elisa; Lira, Alena; Zhou, Mingming; Weisstaub, Noelia; Hen, Rene; Gingrich, Jay A.; Sealfon, Stuart C.

CS Department of Neurology, Mount Sinai School of Medicine,  
New York, NY, 10029, USA  
SO Journal of Neuroscience (2003), 23(26), 8836-8843 CODEN:  
JNRSDS; ISSN: 0270-6474  
PB Society for Neuroscience  
DT Journal  
LA English

AB Most neuropharmacol. agents and many drugs of abuse modulate the activity of heptahelical G-protein-coupled receptors. Although the effects of these ligands result from changes in cellular signaling, their neurobehavioral activity may not \*\*\*correlate\*\*\* with results of in vitro signal transduction \*\*\*assays\*\*\*. 5-Hydroxytryptamine 2A receptor (5-HT2AR) partial agonists that have similar pharmacol. profiles differ in the behavioral responses they elicit. In vitro studies suggest that different agonists acting at the same receptor may establish distinct patterns of signal transduction. \*\*\*Testing\*\*\* this hypothesis in the brain requires a global signal transduction \*\*\*assay\*\*\* that is applicable in vivo. To distinguish the cellular effects of the different 5-HT2AR agonists, we developed an \*\*\*assay\*\*\* for global signal transduction on the basis of high throughput quantification of rapidly modulated transcripts. Study of the responses to agonists in human embryonic kidney 293 cells stably expressing 5-HT2ARs demonstrated that each agonist elicits a distinct transcriptome fingerprint. We therefore studied behavioral and cortical signal transduction responses in wild-type and 5-HT2AR null-mutant mice. The hallucinogenic chems. (+-)-2,5-dimethoxy-4-iodoamphetamine (DOI) and lysergic acid diethylamide (LSD) stimulated a head-twitch behavioral response that was not obsd. with the nonhallucinogenic lisuride hydrogen maleate (LHM) and was absent in receptor null-mutant mice. We also found that DOI, LSD, and LHM each induced distinct transcriptome fingerprints in somatosensory cortex that were absent in 5-HT2AR null-mutants. Moreover, DOI and LSD showed similarities in the transcriptome fingerprints obtained that were not obsd. with the behaviorally inactive drug LHM. Our results demonstrate that chems. acting at the 5-HT2AR induced specific cellular response patterns in vivo that are reflected in unique changes in the somatosensory cortex transcriptome.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:752584 CAPLUS DN 140:175054

TI Expression of drug-metabolizing enzymes, nuclear transcription factors and ABC transporters in Caco-2 cells  
AU Borlak, J.; Zwadlo, C.  
CS Center for Drug Research and Medical Biotechnology, Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover, D-30659, Germany  
SO Xenobiotica (2003), 33(9), 927-943 CODEN: XENOBH; ISSN: 0049-8254  
PB Taylor & Francis Ltd.  
DT Journal  
LA English

AB 1. Caco-2 cells are frequently used in intestinal drug absorption and metab. studies, but little is known about the effects of drugs on the simultaneous expression of genes coding for drug-metabolizing enzymes (DMEs), nuclear transcription factors and ABC transporters. 2. The gene expression and enzyme activities of control and Aroclor 1254-treated cultures were therefore explored, the latter being a powerful inducer of DMEs. Fourteen- and 80-fold induction of CYP1A1 and CYP1A2

mRNA were shown, whereas expression of other DMEs was either increased (CYP2C8-2C19, 10-fold; CYP3A5, twofold; FMO1, 2 and 5, twofold; epoxide hydrolase, threefold) or repressed (CYP2D6 and CYP2E1 to 75% of control values). Notably, gene copies of CYP3A4 and CYP2B6/7 were below the limit of detection, but a three- and 10-fold induction of HNF 1.alpha. + .beta., HNF-4.alpha.4 and a similar 10-fold increase in STAT 3 and 4 was obsd. Similarly, c/EBP transcripts were only detected in treated cell cultures, but MRP1, its isoforms 3-5 as well as MDR-1 were increased threefold after dosing with Aroclor 1254. Overall, CYP gene expression \*\*\*correlated\*\*\* well with the cognate enzyme activity using \*\*\*testosterone\*\*\* as a marker substrate.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:740351 CAPLUS DN 139:359811

TI \*\*\*Expression\*\*\* \*\*\*profiling\*\*\* using cDNA microarrays

AU Zhao, Suling; Bruce, Wesley B.  
SO Pioneer Hi-Bred International, Inc., Johnston, IA, USA  
SO Methods in Molecular Biology (Totowa, NJ, United States) (2003), 236(Plant Functional Genomics), 365-380 CODEN: MMBIED; ISSN: 1064-3745  
PB Humana Press Inc.

DT Journal  
LA English

AB Microarray technol. has become increasingly useful in measuring expression levels of a large no. of genes and part of a repertoire of functional genomic tools. We describe the methods of cDNA microarray prepn., the use, data collection, and initial data processing. The cDNA fragments are first prepd. by polymerase chain reaction (PCR), and then attached to a solid substrate, such as a chem. treated glass slide. Robotic machines spot the prepd. cloned cDNA samples in a miniaturized gridded pattern, so that nanoliter amts. of tens of thousands cDNA samples are bound to a single 7.5 .times. 2.5 cm glass slide. Probes are generated from RNA samples of \*\*\*test\*\*\* and control tissues by incorporating Cyanine dyes (Cy 3 or Cy5) in reverse-transcribed products. Probes from a \*\*\*test\*\*\* sample are labeled with one of two Cy dyes and mixed in equal amts. with probes from a control sample labeled with the second dye. The glass slides contg. the cDNA microarray are hybridized with the mixed Cy-labeled probes, washed, dried, and scanned using laser scanners with an optimized wavelength to excite each Cy dye. The emission image patterns for each dye are captured by a digital camera using micro-optics and processed into numerical values that pos. \*\*\*correlate\*\*\* with quant. levels of mRNA for each cDNA spot on the slide. The collected data is then further processed, normalized across expts., and examd. via numerous statistical and math. approaches to infer changes in expression levels of particular genes due to the treatment \*\*\*tested\*\*\*.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:733779 CAPLUS DN 139:336137

TI Identification of Novel Gene Expression Targets for the Ras Association Domain Family 1 (RASSF1A) Tumor Suppressor Gene in Non-Small Cell Lung Cancer and Neuroblastoma



AU Agathangelou, Angelo; Bieche, Ivan; Ahmed-Choudhury, Jalal; Nicke, Barbara; Dammann, Reinhard; Baksh, Shairaz; Gao, Boning; Minna, John D.; Downward, Julian; Maher, Eamonn R.; Latif, Farida  
CS Division of Reproductive and Child Health, Section of Medical and Molecular Genetics, University of Birmingham, Birmingham, B15 2TT, UK  
SO Cancer Research (2003), 63(17), 5344-5351 CODEN: CNREA8; ISSN: 0008-5472  
PB American Association for Cancer Research  
DT Journal  
LA English  
AB RASSF1A is a recently identified 3p21.3 tumor suppressor gene. The high frequency of epigenetic inactivation of this gene in a wide range of human sporadic cancers including non-small cell lung cancer (NSCLC) and neuroblastoma suggests that RASSF1A inactivation is important for tumor development. Although little is known about the function of RASSF1A, preliminary data suggests that it may have multiple functions. To gain insight into RASSF1A functions in an unbiased manner, the authors have characterized the \*\*\*expression\*\*\* \*\*\*profile\*\*\* of a lung cancer cell line (A549) transfected with RASSF1A. Initially the authors demonstrated that transient expression of RASSF1A into the NSCLC cell line A549 induced G1 cell cycle arrest, as measured by propidium iodide staining. Furthermore, annexin-V staining showed that RASSF1A-expressing cells had an increased sensitivity to staurosporine-induced apoptosis. The authors then screened a cDNA microarray contg. more than 6000 probes to identify genes differentially regulated by RASSF1A. Sixty-six genes showed at least a 2-fold change in expression. Among these were many genes with relevance to tumorigenesis involved in transcription, cytoskeleton, signaling, cell cycle, cell adhesion, and apoptosis. For 22 genes the authors confirmed the microarray results by real-time RT-PCR and/or Northern blotting. In silico, the authors were able to confirm the majority of these genes in other NSCLC cell lines using published data on \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. Furthermore, the authors confirmed 10 genes at the RNA level in two neuroblastoma cell lines, indicating that these RASSF1A target genes have relevance in non-lung cell backgrounds. Protein anal. of six genes (ETS2, Cyclin D3, CDH2, DAPK1, TXN, and CTSL) showed that the changes induced by RASSF1A at the RNA level \*\*\*correlated\*\*\* with changes in protein expression in both non-small cell lung cancer and neuroblastoma cell lines. Finally, the authors have used a transient \*\*\*assay\*\*\* to demonstrate the induction of CDH2 and TGM2 by RASSF1A in NSCLC cell lines. The authors have identified several novel targets for RASSF1A tumor suppressor gene both at the RNA and the protein levels in two different cellular backgrounds. The identified targets are involved in diverse cellular processes; this should help toward understanding mechanisms that contribute to RASSF1A biol. activity.  
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT  
  
L9 ANSWER 34 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:731258 CAPLUS DN 139:378921  
TI Differential expression of DOC-1 in microsatellite-unstable human colorectal cancer  
AU Yuan, Ziqiang; Sotsky Kent, Tara; Weber, Thomas K.  
CS Department of Molecular Genetics, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, 10461, USA

SO Oncogene (2003), 22(40), 6304-6310 CODEN: ONCNES; ISSN: 0950-9232  
PB Nature Publishing Group  
DT Journal  
LA English  
AB The precise genetic mechanism of malignant transformation in DNA mismatch repair deficient, microsatellite-unstable colorectal cancer (CRC) has yet to be elucidated. The authors employed cDNA microarray to identify \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* among CRC cell lines and to compare directly lines with and without microsatellite instability. This study was undertaken to \*\*\*test\*\*\* the hypothesis that microsatellite-unstable CRC cell lines demonstrate specific \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* that differ significantly from those obsd. among microsatellite-stable CRC. Multiple differential expression patterns were identified. Genes demonstrating differential expression included deleted-in-oral-cancer-1 (DOC-1), a highly conserved growth suppressor. DOC-1 expression \*\*\*correlated\*\*\* with microsatellite status, with significantly decreased expression in microsatellite-unstable cell lines and constitutive expression in microsatellite-stable cell lines. The authors also obsd. alterations in the biol. behavior of p12DOC-1-deficient cell lines, with increased S phase and decreased apoptosis compared to microsatellite-stable (DOC-1+) cell lines. Transfection of p12DOC-1 into SW48, which lacks p12DOC-1 expression, resulted in cell cycle and apoptosis profiles similar to other p12DOC-1+ cell lines. These results support the hypothesis that microsatellite-unstable CRC is characterized by novel \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* different from those assocd. with microsatellite-stable CRC, and demonstrate that p12DOC-1 has tumor suppressor potential in colon epithelial cells.  
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT  
  
L9 ANSWER 35 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:729419 CAPLUS DN 139:359401  
TI Expressive genomic hybridization: \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* at the cytogenetic level  
AU Al-Mulla, F.; Al-Maghrebi, M.; Varadharaj, G.  
CS Department of Pathology, Molecular Pathology Unit, Faculty of Medicine, Kuwait University, Safat, 13110, Kuwait  
SO Molecular Pathology (2003), 56(4), 210-217 CODEN: MOPAF6; ISSN: 1366-8714  
PB BMJ Publishing Group  
DT Journal  
LA English  
AB A cytogenetic technique is developed suitable for the rapid assessment of global gene expression that is based on comparative genomic hybridization (CGH), and to use it to understand the relation between genetic amplifications and gene expression. Whereas traditional CGH uses DNA as \*\*\*test\*\*\* and ref. in hybridizations, expressive genomic hybridization (EGH) uses globally amplified mRNA as \*\*\*test\*\*\* and normal DNA as ref. EGH is a rapid and powerful tool for localizing and studying global \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* and \*\*\*correlating\*\*\* them with loci of genetic amplifications using traditional CGH. EGH was used to \*\*\*correlate\*\*\* genetic amplifications detected by CGH with the \*\*\*expression\*\*\* \*\*\*profile\*\*\* of two independent cell lines Colo320 and T47D. Although many amplifications resulted in overexpression, other amplifications were partially or completely silenced at the cytogenetic level. This technique will assist in the anal. of overexpressed genes within amplicons and

could resolve a controversial issue in cancer cytogenetics; namely, the relation between genetic amplifications and overexpression.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 36 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:725980 CAPLUS

DN 139:346474

TI Diametrical clustering for identifying anti- \*\*\*correlated\*\*\* gene clusters

AU Dhillon, Inderjit S.; Marcotte, Edward M.; Roshan, Usman

CS Department of Computer Sciences, University of Texas, Austin, TX, 78712, USA

SO Bioinformatics (2003), 19(13), 1612-1619 CODEN: BOINFP; ISSN: 1367-4803

PB Oxford University Press

DT Journal

LA English

AB Clustering genes based upon their expression patterns allows us to predict gene function. Most existing clustering algorithms cluster genes together when their expression patterns show high pos. \*\*\*correlation\*\*\*. However, it has been obsd. that genes whose expression patterns are strongly anti- \*\*\*correlated\*\*\* can also be functionally similar. Biol., this is not unintuitive-genes responding to the same stimuli, regardless of the nature of the response, are more likely to operate in the same pathways. We present a new diametrical clustering algorithm that explicitly identifies anti- \*\*\*correlated\*\*\* clusters of genes. Our algorithm proceeds by iteratively (i) re-partitioning the genes and (ii) computing the dominant singular vector of each gene cluster; each singular vector serving as the prototype of a 'diametric' cluster. We empirically show the effectiveness of the algorithm in identifying diametrical or anti- \*\*\*correlated\*\*\* clusters. \*\*\*Testing\*\*\* the algorithm on yeast cell cycle data, fibroblast gene expression data, and DNA microarray data from yeast mutants reveals that opposed cellular pathways can be discovered with this method. We present systems whose mRNA expression patterns, and likely their functions, oppose the yeast ribosome and proteosome, along with evidence for the inverse transcriptional regulation of a no. of cellular systems.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:712906 CAPLUS

DN 139:321204

TI Identification of a gene expression signature associated with pediatric AML prognosis

AU Yagi, Tomohito; Morimoto, Akira; Eguchi, Mariko; Hibi, Shigeyoshi; Sako, Masahiro; Ishii, Eiichi; Mizutani, Shuki;

Imashuku, Shinsaku; Ohki, Misao; Ichikawa, Hitoshi

CS Cancer Genomics Division, National Cancer Center Research Institute, Tokyo, Japan

SO Blood (2003), 102(5), 1849-1856 CODEN: BLOOAW; ISSN: 0006-4971

PB American Society of Hematology

DT Journal

LA English

AB Most patients with acute myeloid leukemia (AML) enter complete remission (CR) after treatment with chemotherapy, but a large no. of them experience relapse with resistant disease. To identify genes that are assocd. with their prognoses, we analyzed

gene expression in 54 pediatric patients with AML using an oligonucleotide microarray that contained 12 566 probe sets. A supervised approach using the Student t \*\*\*test\*\*\* selected a prognostic set of 35 genes, some of which are assocd. with the regulation of cell cycle and apoptosis. Most of these genes had not previously been reported to be assocd. with prognosis and were not \*\*\*correlated\*\*\* with morphol. classified French-American-British (FAB) subtypes or with karyotypes. These results indicate the existence of prognosis-assocd. genes that are independent of cell lineage and cytogenetic abnormalities, and they can provide therapeutic direction for individual risk-adapted therapy for pediatric AML patients.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 38 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:709168 CAPLUS

DN 139:321198

TI Molecular classification of breast carcinomas using tissue microarrays

AU Callagy, Grace; Cattaneo, Elena; Daigo, Yataro; Happerfield, Lisa; Bobrow, Lynda G.; Pharoah, Paul D. P.; Caldas, Carlos

CS Cancer Genomics Program, Department of Oncology, Hutchison/MRC Research Centre, University of Cambridge, Cambridge, CB2 2XZ, UK

SO Diagnostic Molecular Pathology (2003), 12(1), 27-34 CODEN: DMPAES; ISSN: 1052-9551

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB The histopathol. classification of breast cancer stratifies tumors based on tumor grade, stage, and type. Despite an overall \*\*\*correlation\*\*\* with survival, this classification is poorly predictive and tumors with identical grade and stage can have markedly contrasting outcomes. Recently, breast carcinomas have been classified by their \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* on frozen material. The validation of such a classification on formalin-fixed paraffin-embedded tumor archives linked to clin. information in a high-throughput fashion would have a major impact on clin. practice. The authors \*\*\*tested\*\*\* the ability of tumor tissue microarrays (TMAs) to sub-classify breast cancers using a TMA contg. 107 breast cancers. The pattern of expression of 13 different protein biomarkers was assessed by immunohistochem. and the multidimensional data was analyzed using an unsupervised two-dimensional clustering algorithm. This revealed distinct tumor clusters which divided into two main groups \*\*\*correlating\*\*\* with tumor grade ( $P < 0.001$ ) and nodal status ( $P = 0.04$ ). None of the protein biomarkers \*\*\*tested\*\*\* could individually identify these groups. The biol. significance of this classification is supported by its similarity with one derived from gene expression microarray anal. Thus, mol. profiling of breast cancer using a limited no. of protein biomarkers in TMAs can sub-classify tumors into clin. and biol. relevant subgroups.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:658858 CAPLUS

DN 139:290048

TI \*\*\*Expression\*\*\* \*\*\*profiling\*\*\* of tumor necrosis factor alpha-induced apoptosis-associated genes in human solid tumor cell lines



AU Yanai, Yoshiaki; Micallef, Mark J.; Yamamoto, Shigeto; Yamamoto, Kozou; Yamauchi, Hiroshi; Ikegami, Hakuo; Kurimoto, Masashi  
CS Fujisaki Institute, Hayashibara Biochemical Laboratories Inc., Okayama, 702-8006, Japan  
SO Anticancer Research (2003), 23(3B), 2339-2348 CODEN: ANTRD4; ISSN: 0250-7005  
PB International Institute of Anticancer Research  
DT Journal  
LA English  
AB Background: The induction of genes assocd. with cellular apoptosis by tumor necrosis factor-alpha (TNF-.alpha.) in human cancer cell lines of various tissue origins may characterize TNF-.alpha. responder cell lines/cancers. Materials and Methods: Using quant. real-time polymerase chain reaction (PCR), the comprehensive mol. profiling of genes downstream of the TNF-.alpha. receptor genes in 91 well-defined human cancer cell lines allowed us to elucidate relationships between TNF-.alpha. response and the genetic \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of the target cell lines. Results: Among the 52 genes \*\*\*tested\*\*\*, the above av. expression of Akt mRNA showed significant \*\*\*correlation\*\*\* with TNF-.alpha.-induced susceptibility to apoptosis. In addn., multidrug resistance protein 5 (MRP5) and tumor necrosis factor receptor type 1 (TNFR1) mRNA expressions also appear to be possible markers for responsiveness to TNF-.alpha.. Conclusion: These results provide a preliminary basis for the screening for genetic markers that may help to predict a favorable therapeutic outcome, and also to identify patients who may benefit from cytokine therapy.  
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 40 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:638806 CAPLUS  
DN 139:285573  
TI Prediction of clinical drug efficacy by classification of drug-induced genomic \*\*\*expression\*\*\* \*\*\*profiles\*\*\* in vitro  
AU Gunther, Erik C.; Stone, David J.; Gerwien, Robert W.; Bento, Patricia; Heyes, Melvyn P.  
CS CuraGen Corporation, Branford, CT, 06405, USA  
SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(16), 9608-9613 CODEN: PNASA6; ISSN: 0027-8424  
PB National Academy of Sciences  
DT Journal  
LA English  
AB \*\*\*Assays\*\*\* of drug action typically evaluate biochem. activity. However, accurately matching therapeutic efficacy with biochem. activity is a challenge. High-content cellular \*\*\*assays\*\*\* seek to bridge this gap by capturing broad information about the cellular physiol. of drug action. Here, we present a method of predicting the general therapeutic classes into which various psychoactive drugs fall, based on high-content statistical categorization of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* induced by these drugs. When we used the classification tree and random forest supervised classification algorithms to analyze microarray data, we derived general "efficacy \*\*\*profiles\*\*\*" of biomarker \*\*\*gene\*\*\* \*\*\*expression\*\*\* that \*\*\*correlate\*\*\* with anti-depressant, antipsychotic and opioid drug action on primary human neurons in vitro. These profiles were used as predictive models to classify naive in vitro drug treatments with 83.3% (random forest) and 88.9% (classification tree) accuracy. Thus, the detailed information contained in genomic expression data is sufficient to match the physiol. effect of a novel drug at the cellular level with

its clin. relevance. This capacity to identify therapeutic efficacy on the basis of gene expression signatures in vitro has potential utility in drug discovery and drug target validation.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 41 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:637863 CAPLUS  
DN 139:241251  
TI Technical advances: Genome-wide cDNA-AFLP analysis of the Arabidopsis transcriptome  
AU Volkmuth, Wayne; Turk, Stefan; Shapiro, Amy; Fang, Yiwen; Kiegle, Ed; Van Haaren, Mark; Donson, Jonathan  
CS Ceres, Inc., Malibu, CA, USA  
SO OMICS (2003), 7(2), 143-159 CODEN: OMICAE; ISSN: 1536-2310  
PB Mary Ann Liebert, Inc.  
DT Journal  
LA English  
AB CDNA-AFLP, a technol. historically used to identify small nos. of differentially expressed genes, was adapted as a genome-wide transcript profiling method. mRNA levels were \*\*\*assayed\*\*\* in a diverse range of tissues from Arabidopsis thaliana plants grown under a variety of environmental conditions. The resulting cDNA-AFLP fragments were sequenced. By linking cDNA-AFLP fragments to their corresponding mRNAs via these sequences, a database was generated that contained quant. expression information for up to two-thirds of gene loci in A. thaliana, ecotype Ws. Using this resource, the expression levels of genes, including those with high nucleotide sequence similarity, could be detd. in a high-throughput manner merely by comparing cDNA-AFLP profiles with the database. The lengths of cDNA-AFLP fragments inferred from their electrophoretic mobilities \*\*\*correlated\*\*\* well with actual fragment lengths detd. by sequencing. In addn., the concns. of AFLP fragments from single cDNAs were highly \*\*\*correlated\*\*\*, illustrating the validity of cDNA-AFLP as a quant., genome-wide, transcript profiling method. CDNA-AFLP profiles were also qual. consistent with mRNA profiles obtained from parallel microarray anal., and with data from previous studies.  
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 42 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:616880 CAPLUS  
DN 139:271590  
TI Gene expression analysis using single molecule detection  
AU Korn, Kerstin; Gardellin, Paola; Liao, Bohao; Amacker, Mario; Bergstroem, Asa; Bjoerkman, Henrik; Camacho, Agnes; Doerhoefer, Sabine; Doerre, Klaus; Enstroem, Johanna; Ericson, Thomas; Favez, Tatiana; Goesch, Michael; Honegger, Adrian; Jaccoud, Sandra; Lapczynska, Markus; Litborn, Erik; Thyberg, Per; Winter, Holger; Rigler, Rudolf  
CS Gnothis AB, Electrum 212, Kista, SE-164 40, Swed.  
SO Nucleic Acids Research (2003), 31(16), e89/1-e89/8 CODEN: NARHAD; ISSN: 0305-1048  
PB Oxford University Press  
DT Journal  
LA English  
AB Recent developments of single mol. detection techniques and in particular the introduction of fluorescence \*\*\*correlation\*\*\* spectroscopy (FCS) led to a no. of important applications in biol. research. We present a unique approach for the gene expression anal. using dual-color cross-

\*\*\*correlation\*\*\* . The expression \*\*\*assay\*\*\* is based on gene-specific hybridization of two dye-labeled DNA probes to a selected target gene. The counting of the dual-labeled mols. within the soln. allows the quantification of the expressed gene copies in abs. nos. As detection and anal. by FCS can be performed at the level of single mols., there is no need for any type of amplification. We describe the gene expression \*\*\*assay\*\*\* and present data demonstrating the capacity of this novel technol. In order to prove the gene specificity, we performed expts. with gene-depleted total cDNA. The biol. application was demonstrated by quantifying selected high, medium and low abundant genes in cDNA prep. from HL-60 cells.  
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 43 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:601882 CAPLUS  
DN 139:243916  
TI MLANA/MART1 and SILV/PMEL17/GP100 are transcriptionally regulated by MITF in melanocytes and melanoma  
AU Du, Jinyan; Miller, Arlo J.; Widlund, Hans R.; Horstmann, Martin A.; Ramaswamy, Sridhar; Fisher, David E.  
CS Department of Pediatric Hematology/Oncology, Harvard Medical School, Boston, USA  
SO American Journal of Pathology (2003), 163(1), 333-343 CODEN: AJPA44; ISSN: 0002-9440  
PB American Society for Investigative Pathology  
DT Journal  
LA English  
AB The clin. important melanoma diagnostic antibodies HMB-45, melan-A, and MrfF (D5) recognize gene products of the melanocyte-lineage genes SILV/PMEL17/GP100, MLANA/MART1, and MITF, resp. MITF encodes a transcription factor that is essential for normal melanocyte development and appears to regulate expression of several pigmentation genes. In this report, the possibility was examd. that MITF might addnl. regulate expression of the SILV and MLANA genes. Both genes contain conserved MITF consensus DNA sequences that were bound by MITF in vitro and in vivo, based on electrophoretic mobility shift \*\*\*assay\*\*\* and chromatin-immunopptn. In addn., MITF regulated their promoter/enhancer regions in reporter \*\*\*assays\*\*\*, and up- or down-regulation of MITF produced corresponding modulation of endogenous SILV and MLANA in melanoma cells. Expression patterns were compared with these factors in a series of melanoma cell lines whose mutational status of the proto-oncogene BRAF was also known. SILV and MLANA expression \*\*\*correlated\*\*\* with MITF, while no clear \*\*\*correlation\*\*\* was seen relative to BRAF mutation. Finally, mRNA expression array anal. of primary human melanomas demonstrated a tight \*\*\*correlation\*\*\* in their expression levels in clin. tumor specimens. Collectively, this study links three important melanoma antigens into a common transcriptional pathway regulated by MITF.  
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 44 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:598331 CAPLUS  
DN 140:70456  
TI Identification of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* predicting tumor cell response to L-alanosine  
AU Efferth, Thomas; Gebhart, Erich; Ross, Douglas D.; Sauerbrey, Axel

CS Center for Molecular Biology, University of Heidelberg, Heidelberg, 69120, Germany  
SO Biochemical Pharmacology (2003), 66(4), 613-621 CODEN: BCPA6; ISSN: 0006-2952  
PB Elsevier Science B.V.  
DT Journal  
LA English  
AB The methylthioadenosine phosphorylase (MTAP) gene gained considerable interest as therapeutic target for tumors with the 9p21 deletion. This gene maps to 9p21 and loss of this chromosomal region in tumors offers an unique opportunity for chemoselective treatment, since MTAP is an important salvage enzyme for the formation of adenine that is needed for DNA synthesis. L-Alanosine, an antibiotic from Streptomyces alanosinicus, blocks the common de novo purine biosynthesis pathway and, thereby, inhibits tumor cells with MTAP deficiency. Normal cells escape the detrimental effects of L-alanosine due to their proficiency in the MTAP salvage pathway. The present anal. was undertaken to gain insights into the mol. architecture of tumor cells that det. the response to L-alanosine apart from the MTAP gene. Anal. of cell doubling times and IC50 values for L-alanosine showed that slowly growing cell lines were more resistant to L-alanosine than rapidly growing ones. Mining the database of the National Cancer Institute (N.C.I.), for the mRNA expression of 9706 genes in 60 cell lines by means of Kendall's .tau.- \*\*\*test\*\*\*, false discovery rate calcn., and hierarchical cluster anal. pointed to 11 genes or expressed sequence tags whose mRNA expression \*\*\*correlated\*\*\* with the IC50 values for L-alanosine. Furthermore, we \*\*\*tested\*\*\* L-alanosine for cross-resistance in multidrug-resistant cell lines which overexpress selectively either the P-glycoprotein/MDR1 (CEM/ADR5000), MRP1 (HL-60/AR), or BCRP (MDA-MB-231-BCRP) genes. None of the multidrug-resistant cell lines was cross-resistant to L-alanosine indicating that L-alanosine may be suitable to treat multidrug-resistant, refractory tumors in the clinic. Finally, the IC50 values for L-alanosine of the 60 cell lines were \*\*\*correlated\*\*\* to the p53 mutational status and expression of p53 downstream genes. We found that p53 mutated cell lines were more resistant to L-alanosine than p53 wild type cell lines.  
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 45 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:595424 CAPLUS  
DN 140:104572  
TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* for the prediction of therapeutic response to docetaxel in patients with breast cancer  
AU Chang, Jenny C.; Wooten, Eric C.; Tsimelzon, Anna; Hilsenbeck, Susan G.; Gutierrez, M. Carolina; Elledge, Richard; Mohsin, Syed; Osborne, C. Kent; Chamness, Gary C.; Allred, D. Craig; O'Connell, Peter  
CS Breast Center and the Departments of Medicine, Pathology, and Molecular and Cellular Biology, Methodist Hospital, Baylor College of Medicine, Houston, TX, 77030, USA  
SO Lancet (2003), 362(9381), 362-369 CODEN: LANCAO; ISSN: 0140-6736  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
AB Systemic chemotherapy for operable breast cancer substantially decreases the risk of death. Patients often have de novo resistance or incomplete response to docetaxel, one of the most active agents in this disease. We postulated that

\*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of the primary breast cancer can predict the response to docetaxel. We took core biopsy samples from primary breast tumors in 24 patients before treatment and then assessed tumor response to neoadjuvant docetaxel (four cycles, 100 mg/m<sup>2</sup> daily for 3 wk) by cDNA anal. of RNA extd. from biopsy samples using Hgu95-Av2 GeneChip. From the core biopsy samples, we extd. sufficient total RNA (3-6 .mu.g) for cDNA array anal. using Hgu95-Av2 GeneChip. Differential patterns of expression of 92 genes \*\*\*correlated\*\*\* with docetaxel response (p=0.cntdot.001). Sensitive tumors had higher expression of genes involved in cell cycle, cytoskeleton, adhesion, protein transport, protein modification, transcription, and stress or apoptosis; whereas resistant tumors showed increased expression of some transcriptional and signal transduction genes. In leave-one-out cross-validation anal., ten of 11 sensitive tumors (90% specificity) and 11 of 13 resistant tumors (85% sensitivity) were correctly classified, with an accuracy of 88%. This 92-gene predictor had pos. and neg. predictive values of 92% and 83%, resp. \*\*\*Correlation\*\*\* between RNA expression measured by the arrays and semiquant. RT-PCR was also ascertained, and our results were validated in an independent set of six patients. If validated, these mol. profiles could allow development of a clin. \*\*\*test\*\*\* for docetaxel sensitivity, thus reducing unnecessary treatment for women with breast cancer.  
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 46 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:591440 CAPLUS  
DN 139:148006  
TI Comparative gene profiling between undifferentiated and well-differentiated nasopharyngeal carcinoma (NPC) cells for NPC diagnosis and treatment  
IN Ng, Aylwin; Tang, Jing P.; Hui, Kam M.; Goh, Christopher H. K.  
PA Biotech Research Ventures Pte Limited, Singapore; Cripps, Joanna E.  
SO PCT Int. Appl., 61 pp. CODEN: PIXXD2  
DT Patent  
LA English

FAN.CNT 1 PATENT NO.	KIND	DATE	APPLICATION NO.
NO.	DATE	-----	-----
PI WO 2003062826	A2	20030731	WO 2003-GB329
20030123 WO 2003062826	A3	20031016	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
PRAI GB 2002-1498	A	20020123	

AB The invention is concerned with the detection and treatment of nasopharyngeal carcinoma (NPC) based on differential gene expression in these cells. Specifically, the invention provides details of differentially expressed genes in NPC which serve to detect the presence or risk of the disease and its clin. type. A set of genes are identified by DNA microarray using comparative gene profiling between undifferentiated and well-differentiated

nasopharyngeal carcinoma (NPC) cells (CNE-2 or HK1 resp.) to be assocd. with NPC, in particular, two imprinted genes H19 (no protein product, function unknown) and CDKN1C (cyclin-dependent kinase inhibitor 1C) located on chromosome 11p15. It is also shown H19 gene is highly expressed in CNE-2 cells and hypermethylation of its CpG promoter region is detected in the HK1 cells. Furthermore, hypomethylation of the CpG dinucleotides within H19 promoter region is \*\*\*correlated\*\*\* with the restoration of its mRNA expression in HK1 cells. The invention also provides methods of treating NPC in assocn. with chemo or radiotherapy.

L9 ANSWER 47 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:587616 CAPLUS  
DN 139:192391  
TI GATA-1 \*\*\*testis\*\*\* activation region is essential for Sertoli cell-specific expression of GATA-1 gene in transgenic mouse  
AU Wakabayashi, Junko; Yomogida, Kentaro; Nakajima, Osamu; Yoh, Keigyou; Takahashi, Satoru; Engel, James Douglas; Ohneda, Kinuko; Yamamoto, Masayuki  
CS Centre for Tsukuba Advanced Research Alliance, University of Tsukuba, Tsukuba, 305-8577, Japan  
SO Genes to Cells (2003), 8(7), 619-630 CODEN: GECEFL; ISSN: 1356-9597  
PB Blackwell Publishing Ltd.  
DT Journal  
LA English

AB The erythroid transcription factor GATA-1 is also expressed in Sertoli cells of the \*\*\*testis\*\*\*. The \*\*\*testicular\*\*\* expression of GATA-1 is regulated in a developmental and spermatogenic stage-specific manner. To further clarify the regulatory mechanisms of \*\*\*testicular\*\*\* GATA-1 gene expression, we carried out transgenic reporter gene expression analyses. We found that GATA-1 expression in Sertoli cells is markedly decreased concomitant with the emergence of elongated spermatids in the seminiferous tubules. Transgenic reporter mouse analyses revealed that a 15 kb GATA-1 genomic region is sufficient to recapitulate the \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* in Sertoli cells. While the GATA-1 haematopoietic enhancer and the proximal first exon are included within the 15 kb genomic region, these regulatory elements are not essential for GATA-1 expression in Sertoli cells. Further analyses using deletion constructs revealed that a 1.5 kb region 5' to the GATA-1 haematopoietic enhancer is essential for gene expression in Sertoli cells and this region is referred to as the GATA-1 \*\*\*testis\*\*\* activation region. These results thus demonstrated that the GATA-1 \*\*\*testis\*\*\* activation region is essential for Sertoli cell-specific expression of GATA-1 gene. The 15 kb genomic region is applicable and useful for the expression vector system specific for adult Sertoli cells in stage VII to IX.  
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 48 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:579796 CAPLUS  
DN 139:271563  
TI Gene Expression Analysis of the Acute Phase Response Using a Canine Microarray  
AU Higgins, M. A.; Berridge, B. R.; Mills, B. J.; Schultze, A. E.; Gao, H.; Searfoss, G. H.; Baker, T. K.; Ryan, T. P.  
CS Department of Lead Optimization Toxicology, Lilly Res. Laboratories, Greenfield, IN, 46140, USA

SO Toxicological Sciences (2003), 74(2), 470-484 CODEN:  
TOSCF2; ISSN: 1096-6080  
PB Oxford University Press  
DT Journal  
LA English

AB The safety of pharmaceuticals is typically assessed in the dog and rat prior to investigation in humans. As a result, a greater understanding of adverse effects in these preclin. **\*\*\*testing\*\*\*** species would improve safety assessment. Despite this need, there is a lack of tools to examine mechanisms and identify biomarkers in the dog. To address this issue, we developed an Affymetrix-based oligonucleotide microarray capable of monitoring the expression of thousands of canine genes in parallel. The custom canine array contains 22,774 probe sets, consisting of 13,729 canine and 9045 human-derived probe sets. To improve cross-species hybridization with human-derived probes, the detection region was moved from the variable 3' UTR to the more homologous coding region. **\*\*\*Testing\*\*\*** of this strategy was accomplished by comparing hybridization of naive dog liver RNA to the canine array (coding region design) and human U133A array (std. 3' design). Although raw signal intensity was greater with canine-specific probe sets, human-derived probes detected the expression of addnl. liver transcripts. To assess the ability of this tool to detect differential gene expression, the acute phase response was examd. in beagle dogs given lipopolysaccharide (LPS). Hepatic gene expression 4 and 24 h post-LPS administration was compared to **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** **\*\*\*profiles\*\*\*** of vehicle-treated dogs (n = 3/group). Array data was consistent with an acute inflammatory response, with transcripts for multiple cytokines and acute phase proteins markedly induced 4 h after LPS challenge. Robust changes in the expression of transcripts involved with glucose homeostasis, biotransformation, and extracellular matrix remodeling were obsd. 24 h post-dose. In addn., the canine array identified several potential biomarkers of hepatic inflammation. Strong **\*\*\*correlations\*\*\*** were found between gene expression data and alterations in clin. chem. parameters such as serum amyloid A (SAA), albumin, and alk. phosphatase (ALP). In summary, this new genomic tool successfully detected basal canine gene expression and identified novel aspects of the acute phase response in dog that shed new light on mechanisms underlying inflammatory processes.

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 49 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:570529 CAPLUS  
DN 139:111616

TI Differentially expressed nucleic acids and their uses in compositions, kits, and methods for identification, assessment, prevention and therapy of cervical cancer  
IN Schlegel, Robert; Chen, Yan; Deeds, James D.; Zhao, Xumei; Bryant, Barbara Moore  
PA Millennium Pharmaceuticals, Inc., USA  
SO U.S. Pat. Appl. Publ., 44 pp. CODEN: USXXCO  
DT Patent  
LA English

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE				
PI	US 2003138792	A1	20030724	US 2002-161469	
	20020531				
PRAI	US 2001-295144P	P	20010531		

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating cervical cancers. Two hundred twenty-six marker genes are identified through transcriptional profiling expts. on human cervical tissues; these marker genes are over-expressed in squamous cell carcinomas and/or in adenocarcinomas compared with the ectocervix, endocervix, and CIN 1 (cervical intraepithelial neoplasia) tissues. Thus, changes in the levels of expression of one or more of the marker genes is **\*\*\*correlated\*\*\*** with the presence of cervical cancer. Marker gene sets are also provided such that each marker gene set detects a greater no. of cervical cancer patients than that detected by each component marker gene individually.

L9 ANSWER 50 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:557066 CAPLUS  
DN 139:243871

TI Transcriptional Silencing of Zinc Finger Protein 185 Identified by **\*\*\*Expression\*\*\*** **\*\*\*Profiling\*\*\*** Is Associated with Prostate Cancer Progression

AU Vanaja, Donkena Krishna; Cheville, John C.; Iturria, Steve J.; Young, Charles Y. F.

CS Department of Urology, Mayo Clinic/Foundation, Rochester, MN, 55905, USA

SO Cancer Research (2003), 63(14), 3877-3882 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research  
DT Journal  
LA English

AB We profiled the expression of genes in benign and untreated human prostate cancer tissues using oligonucleotide microarrays. We report here 50 genes with distinct expression patterns in metastatic and confined tumors (Gleason score 6 and 9; lymph node invasive and noninvasive). Validation of **\*\*\*expression\*\*\*** **\*\*\*profiles\*\*\*** of 6 genes by quant. PCR revealed a strong inverse **\*\*\*correlation\*\*\*** in the expression of zinc finger protein 185 (ZNF185), bullous pemphigoid antigen gene (BPAG1), and prostate secretory protein (PSP94) with progression of prostate cancer. Treatment of prostate cancer cell lines with 5-aza-2'-deoxycytidine (5-Aza-CdR), an inhibitor of DNA methylation, restored ZNF185 expression levels. Moreover, methylation-specific PCR confirmed methylation of the 5'CpG islands of the ZNF185 gene in all of the metastatic tissues and 44% of the localized tumor tissues, as well as in the prostate cancer cell lines **\*\*\*tested\*\*\***. Thus, transcriptional silencing of ZNF185 by methylation in prostate tumor tissues implicates the ZNF185 gene in prostate tumorigenesis.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 51 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:555423 CAPLUS  
DN 139:144881

TI A global transcriptional regulatory role for c-Myc in Burkitt's lymphoma cells

AU Li, Zirong; Van Calcar, Sara; Qu, Chunxu; Cavenee, Webster K.; Zhang, Michael Q.; Ren, Bing

CS Ludwig Institute for Cancer Research, University of California at San Diego School of Medicine, La Jolla, CA, 92093-0653, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(14), 8164-8169 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences  
DT Journal  
LA English

AB Overexpression of c-Myc is one of the most common alterations in human cancers, yet it is not clear how this transcription factor acts to promote malignant transformation. To understand the mol. targets of c-Myc function, we have used an unbiased genome-wide location-anal. approach to examine the genomic binding sites of c-Myc in Burkitt's lymphoma cells. We find that c-Myc together with its heterodimeric partner, Max, occupy >15% of gene promoters \*\*\*tested\*\*\* in these cancer cells. The DNA binding of c-Myc and Max \*\*\*correlates\*\*\* extensively with gene expression throughout the genome, a hallmark attribute of general transcription factors. The c-Myc/Max heterodimer complexes also colocalize with transcription factor IID in these cells, further supporting a general role for overexpressed c-Myc in global gene regulation. In addn., transcription of a majority of c-Myc target genes exhibits changes \*\*\*correlated\*\*\* with levels of c-myc mRNA in a diverse set of tissues and cell lines, supporting the conclusion that c-Myc regulates them. Taken together, these results suggest a general role for overexpressed c-Myc in global transcriptional regulation in some cancer cells and point toward mol. mechanisms for c-Myc function in malignant transformation.  
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 52 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:542714 CAPLUS  
DN 139:163169  
TI High expression of complement components in omental adipose tissue in obese men  
AU Gabrielson, Britt G.; Johansson, Jenny M.; Loenn, Malin; Jernas, Margareta; Olbers, Torsten; Peltonen, Markku; Larsson, Ingrid; Loenn, Lars; Sjoestroem, Lars; Carlsson, Bjoern; Carlsson, Lena M. S.  
CS Research Centre for Endocrinology and Metabolism, Goeteborg University, Goeteborg, Swed.  
SO Obesity Research (2003), 11(6), 699-708 CODEN: OBREFR; ISSN: 1071-7323  
PB North American Association for the Study of Obesity  
DT Journal  
LA English  
AB Objective: Accumulation of visceral fat is recognized as a predictor of obesity-related metabolic disturbances. Factors that are predominantly expressed in this depot could mediate the link between visceral obesity and assocd. diseases. Research Methods and Procedures: Paired s.c. and omental adipose tissue biopsies were obtained from 10 obese men. Gene expression was analyzed by DNA microarrays in triplicate and by real-time polymerase chain reaction. Serum C3 and C4 were analyzed by radial immunodiffusion \*\*\*assays\*\*\* in 91 subjects representing a cross section of the general population. Body compn. was measured by computerized tomog. Results: Complement components C2, C3, C4, C7, and Factor B had higher expression in omental compared with s.c. adipose tissue (.apprx.2-, 4-, 17-, 10-, and 7-fold, resp.). In addn., adipsin, which belongs to the alternative pathway, and the classical pathway components C1QB, C1R, and C1S were expressed in both depots. Anal. of tissue distribution showed high expression of C2, C3, and C4 in omental adipose tissue, and only liver had higher expression of these genes. Serum C3 levels \*\*\*correlated\*\*\* with both visceral and s.c. adipose tissue in both men ( $r = 0.65$  and  $p < 0.001$  and  $r = 0.52$  and  $p < 0.001$ , resp.) and women ( $r = 0.34$  and  $p = 0.023$  and  $r = 0.49$  and  $p < 0.001$ , resp.), whereas C4 levels \*\*\*correlated\*\*\* with only visceral fat in men ( $r = 0.36$ ,  $p = 0.015$ ) and with both depots in women (visceral:  $r = 0.58$ ,  $p < 0.001$ ; and s.c.:  $r = 0.51$ ,  $p <$

0.001). Discussion: Recent studies show that the metabolic syndrome is assocd. with chronically elevated levels of several immune markers, some of which may have metabolic effects. The high expression of complement genes in intra-abdominal adipose tissue might suggest that the complement system is involved in the development of visceral adiposity and/or contributes to the metabolic complications assocd. with increased visceral fat mass.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 53 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:540544 CAPLUS  
DN 139:348311  
TI Wnt signaling during development of the gastrointestinal tract  
AU Theodosiou, Nicole A.; Tabin, Clifford J.  
CS Department of Genetics, Harvard Medical School, Boston, MA, 02115, USA  
SO Developmental Biology (San Diego, CA, United States) (2003), 259(2), 258-271 CODEN: DEBIAO; ISSN: 0012-1606  
PB Elsevier  
DT Journal  
LA English  
AB Wnt signaling pathways have been demonstrated to play important roles in controlling tissue patterning and cell proliferation. In the gastrointestinal tract, mutations that lead to activation of the canonical Wnt pathway through .beta.-catenin result in familial and sporadic colon cancers. The downstream transcription factor Tcf4 is required to maintain the proliferative stem cell compartment in the crypts of the small intestine. Activation of TCF-dependent transcription is a good \*\*\*correlate\*\*\* to neoplastic transformation. Despite its assocn. with cancer in the colon, little is known of the role for Wnt signaling during development and patterning of the gut tube. We conducted a comprehensive expression screen for Wnt signaling components during different stages of gut development in the chick. Conserved expression patterns of these genes indicate that they likely play essential roles in gut morphogenesis. Based on the \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of putative components of each pathway, we are able to postulate specific roles for the various pathways during gut development. Predictions of roles for canonical signaling in the developing gizzard, duodenum, and large intestine in chick were \*\*\*tested\*\*\* by viral misexpression of dominant-neg. (DN) forms of the downstream cofactors Tcf4 and Lef1. In the chick, Tcf4 is expressed in the posterior gizzard mesoderm. Misexpression of DN-Tcf4 in the splanchnic mesoderm resulted in the failure of the gizzard epithelium to form microvilli. Lef1 is expressed in the chick duodenum and large intestine mesoderm. Viral misexpression of DN-Lef1 resulted in diminished mesoderm and over-proliferation of the large intestine endoderm, leading to stenosis of the lumen. The results from these misexpression studies in the chick, together with evidence from colorectal lesions, indicate that the canonical Wnt pathway plays crit. roles in balancing cell proliferation vs. cell differentiation during gut development. The \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of the Wnt signaling components presented in this paper should prove valuable in deciphering addnl. roles of the Wnt pathways during patterning of the vertebrate gut tube.  
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 54 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:536679 CAPLUS

DN 139:83061

TI A multigene expression panel for the molecular diagnosis of Barrett's esophagus

AU Brabender, J.; Schneider, P. M.; Metzger, R.; Danenberg, K. D.; Danenberg, P. V.; Lord, R. V.; Marjoram, P.; Hoelscher, A. H.

CS Klinik und Poliklinik fuer Visceral- und Gefaesschirurgie, Universitaet Koeln, Cologne, Germany

SO Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2003) 51-53 CODEN: CFEKA7; ISSN: 0303-6227

PB Springer-Verlag

DT Journal

LA German

AB Studies of the genetic basis of the Barrett's metaplasia, dysplasia, adenocarcinoma sequence have mostly investigated small nos. of genes with a limited \*\*\*correlation\*\*\* between the genetic and the clin. or histopathol. findings. The aim of this study was to evaluate whether different Barrett's histopathol. stage tissues could be discriminated by analyzing the data from a large panel of genes using software developed for array systems. 98 Frozen esophageal tissues collected from 19 patients with Barrett's esophagus (BE) and 20 patients with Barrett's - assocd. esophageal adenocarcinoma (EA) were studied. A quant. real-time RT-PCR method (TaqMan) was used to measure, relative to the internal std. beta actin, the mRNA expression levels of the following 23 genes: c-Myb, ODC, CDX2, DNMT1, DNMT3a, DNMT3b, RXRalpha, RXRbeta, RXRgamma, RARalpha, RARgamma, BFT, GSTPI, COX1, COX2, DPD, SPARC, BCL2, TP, BAX, DAPK, TM4SF3, TSPAN. Median mRNA gene expression levels were significantly decreased in adenocarcinomas of the esophagus compared to Barrett's esophagus for: BFT ( $p < 0.001$ ), RXRa ( $p < 0.001$ ), RXRb ( $p = 0.018$ ), RARg ( $p = 0.035$ ), GSTPI ( $p = 0.005$ ), BAX ( $p = 0.009$ ), DAPK ( $p = 0.005$ ), TM4SF3 ( $p = 0.028$ ), TSPAN ( $p < 0.001$ ), and significantly increased in EA compared to BE for: COX2 ( $p = 0.003$ ), RARa ( $p = 0.009$ ), DNMT3b ( $p = 0.021$ ), and SPARC ( $p < 0.001$ ; all Mann-Whitney \*\*\*test\*\*\*). A blinded linear discriminant anal. was able to distinguish four genetically different groups. Two of these groups consisted solely of normal squamous esophagus tissues from patients with BE or EA. The other 2 groups consisted of Barrett's and adenocarcinoma tissues that were statistically very distinct. Complete (100%) sepn. of Barrett's esophagus and cancer tissues could be achieved using the most discriminant genes detd. by logistic regression anal. A non-array parallel mRNA quantitation anal. of a panel of genes using array-type logistic regression and linear discriminant analyses can distinguish between different Barrett's histologies. Further studies to det. the potential clin. value of this approach are warranted.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 55 OF 169 CAPLUS COPYRIGHT 2005 ACS ON STN

AN 2003:528782 CAPLUS

DN 139:274702

TI \*\*\*Gene\*\*\* \*\*\*Expression\*\*\* \*\*\*Profiles\*\*\*

Obtained from Fine-Needle Aspirations of Breast Cancer Reliably Identify Routine Prognostic Markers and Reveal Large-Scale Molecular Differences between Estrogen-negative and Estrogen-positive Tumors

AU Pusztai, Lajos; Ayers, Mark; Stec, James; Clark, Edward; Hess, Kenneth; Stivers, David; Damokosh, Andrew; Sneige, Nour; Buchholz, Thomas A.; Esteve, Francisco J.; Arun, Banu; Cristofanilli, Massimo; Booser, Daniel; Rosales, Marguerite;

Valero, Vicente; Adams, Constantine; Hortobagyi, Gabriel N.; Symmans, W. Fraser

CS Departments of Breast Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030-009, USA

SO Clinical Cancer Research (2003), 9(7), 2406-2415 CODEN: CCREFA; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB PURPOSE: The purpose of this study was to det. whether comprehensive transcriptional profiles (TPs) can be obtained from single-passage fine-needle aspirations (FNAs) of breast cancer and to explore whether profiles capture routine clinicopathol. parameters. Exptl. Design: \*\*\*Expression\*\*\* \*\*\*profiles\*\*\* were available on 38 patients with stage I-III breast cancer who underwent FNA at the time of diagnosis. [33P]dCTP-labeled cDNA probes were generated and hybridized to cDNA membrane microarrays that contained 30,000 human sequence clones, including 10,890 expressed sequence tags. RESULTS: The median total RNA yield from the biopsies was 2 .mu.g (range, 1-25 .mu.g). The cellular compn. of each biopsy was examd. and, on av., 79% of the cells were cancer cells. TP was successfully performed on all 38 of the biopsies. Unsupervised complete-linkage hierarchical clustering with all of the biopsies revealed an assocn. between estrogen receptor (ER) status and \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. There was a strong \*\*\*correlation\*\*\* between ER status detd. by TP and measured by routine immunohistochem. ( $P = 0.001$ ). A similar strong \*\*\*correlation\*\*\* was seen with HER-2 status detd. by fluorescent in situ hybridization ( $P = 0.0002$ ). Using the first 18 cases as the discovery set, we established a cutoff of 2.0 and 18.0 for ER and HER-2 mRNA levels, resp., to distinguish clin.-neg. from -pos. cases. We also identified 105 genes (excluding the ER gene) the expression of which \*\*\*correlated\*\*\* highly with clin. ER status. Twenty tumors were used for prospective validation. HER-2 status was correctly identified in all 20 of the cases, based on HER-2 mRNA content detected by TP. ER status was correctly identified in 19 of 20 cases. When the marker set of 105 genes was used to prospectively predict ER status, TP-based classification correctly identified 9 of 10 of the ER-pos. and 7 of 10 of the ER-neg. tumors. We also explored supervised cluster anal. using various functional categories of genes, and we obsd. a clear sepn. between ER-neg. and ER-pos. tumors when genes involved in signal transduction were used for clustering. CONCLUSIONS: These results demonstrate that comprehensive TP can be performed on FNA biopsies. TPs reliably measure conventional single-gene prognostic markers such as ER and HER-2. A complex pattern of genes (not including ER) can also be used to predict clin. ER status. These results demonstrate that needle biopsy-based diagnostic microarray \*\*\*tests\*\*\* may be developed that could capture conventional prognostic information but may also contain addnl. clin. information that cannot currently be measured with other methods.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 56 OF 169 CAPLUS COPYRIGHT 2005 ACS ON STN

AN 2003:524101 CAPLUS

DN 139:31192

TI Neurokinin 1 receptors and neprilysin modulation of mouse bladder gene regulation

AU Dozmorov, Igor; Saban, Marcia R.; Gerard, Norma P.; Lu, Bao; Nguyen, Ngoc-Bich; Centola, Michael; Saban, Ricardo



CS Oklahoma Medical Research Foundation, Microarray Research Facility, Univ. of Oklahoma Health Sciences Center, Oklahoma City, OK, 73104, USA  
SO Physiological Genomics (2003), 12(3), 239-250 CODEN: PHGEFP; ISSN: 1094-8341 URL: <http://physiolgenomics.physiology.org/cgi/reprint/12/3/239.pdf>  
PB American Physiological Society  
DT Journal; (online computer file)  
LA English

AB Neurokinin 1 (NK1) receptors play a fundamental role in neurogenic inflammation. the authors sought to det. the mechanisms downstream from NK1 receptor (NK1R) activation using cDNA arrays and a novel statistical method to analyze gene expression. The authors used female NK1R-/- and wild-type (WT) mice that were sensitized actively by i.p. injections of dinitrophenol 4 (DNP4)-human serum albumin. Cystitis was induced by intravesical instillation of antigen of DNP4-ovalbumin, and control mice were challenged with saline. At 1, 4, and 24 h after instillation, bladders were removed for RNA extrn. (n = 3), replicate of RNA extrn. (n = 3), and morphol. anal. (n = 6). For cDNA array expts., three bladders from each group were homogenized, and total RNA was obtained. DNase-treated RNA was reverse-transcribed to cDNA, labeled with [ $\alpha$ -<sup>32</sup>P]dATP and hybridized to Atlas Mouse 1.2 Arrays. After calcg. the mean and SD for background spots, each exptl. value was assigned a normalized score S using the formula  $S' = (S - Av)/SD$ , where S' is the original pixel value, and Av and SD are the mean and std. deviation of background spots, resp. Only genes that expressed 3 SD values above background were used. Hypervariable genes were sorted by cluster anal. Matrixes of \*\*\*correlation\*\*\* coeffs. were calcd. and represented in a connectivity mosaic. As results, the authors found that in WT mice the most prominent gene cluster had neprilysin in a central position and pos. \*\*\*correlated\*\*\* to a group of activator protein-1 (AP-1)-responsive genes, including laminin- $\alpha$ 3, tissue plasminogen activator 11, fos-B, and TNF- $\beta$ . In WT mice, antigen-induced bladder inflammation led to a downregulation in neprilysin expression. In contrast, NK1R-/- mice failed to mount an inflammatory reaction and presented neprilysin neg. \*\*\*correlated\*\*\* with the same genes described in WT. In conclusion, this work indicates an overriding participation of NK1R and neprilysin in bladder inflammation, provides a working model for the involvement of AP-1 transcription factor, and evokes \*\*\*testable\*\*\* hypotheses regarding the role of NK1R and neprilysin in inflammation.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 57 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:500231 CAPLUS  
DN 139:161876  
TI Relationship between G+C content, ORF-length and mRNA concentration in *Saccharomyces cerevisiae*  
AU Marin, Antonio; Gallardo, Mercedes; Kato, Yuki; Shirahige, Katsuhiko; Gutierrez, Gabriel; Ohta, Kunihiro; Aguilera, Andres  
CS Departamento de Genetica, Facultad de Biologia, Universidad de Sevilla, Seville, 41012, Spain  
SO Yeast (2003), 20(8), 703-711 CODEN: YESTE3; ISSN: 0749-503X  
PB John Wiley & Sons Ltd.  
DT Journal  
LA English

AB RNA biogenesis is a tightly-regulated process. The levels and timing of expression of a gene depends on its particular function. However, gene expression levels may also depend on

structural features. Here we describe the anal. of gene expression of 4977 ORFs using DNA microarrays covering the whole genome of three different *S. cerevisiae* strains, wild-type and *tho2* and *thp1* mutants with a general effect on mRNA biogenesis. We show that transcripts from G+C-rich ORFs accumulate at higher concns. than those from G+C-poor ones, in different ORF-length categories in all strains \*\*\*tested\*\*\*. In addn., we found a neg. \*\*\*correlation\*\*\* between ORF length and G+C content. Our results indicate that length and G+C content of a gene have a clear effect on its levels of expression. We discuss the biol. relevance of these results, as well as different ways that these structural features could modulate mRNA biogenesis.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 58 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:480579 CAPLUS  
DN 139:318563  
TI Altered Gene Expression during Rat Wolffian Duct Development in Response to in Utero Exposure to the Antiandrogen Linuron  
AU Turner, Katie J.; McIntyre, Barry S.; Phillips, Suzanne L.; Barlow, Norman J.; Bowman, Christopher J.; Foster, Paul M. D.  
CS CIIT Centers for Health Research, Research Triangle Park, NC, 27709-2137, USA  
SO Toxicological Sciences (2003), 74(1), 114-128 CODEN: TOSCF2; ISSN: 1096-6080  
PB Oxford University Press  
DT Journal  
LA English

AB Linuron is an herbicide with weak androgen receptor (AR) antagonist activity. Exposure to linuron from gestation days (GD) 12 to 21 perturbs androgen-dependent male reproductive development. In utero exposure to 50-mg/kg/day linuron induces malformations of the epididymis and the vas deferens. The objective of this study was to identify alterations in gene expression within the \*\*\*testis\*\*\* and epididymis assocd. with abnormal Wolffian duct development and to \*\*\*correlate\*\*\* changes in gene expression with the gross morphol. of the affected epididymides. Pregnant Sprague-Dawley rats were administered either corn oil vehicle or linuron (50 mg/kg/day) by gavage from GD 12 to 21 (n = 3-6 controls, n = 5-10 linuron-treated dams per time point). Changes in gene expression were evaluated in \*\*\*testes\*\*\* on GD 21 and in epididymides on GD 21 and postnatal day (PND) 7, using cDNA microarrays and confirmed by real-time reverse transcriptase PCR (RT-PCR) analyses. RNA was isolated from intact epididymides with reduced or no ductal coiling from the linuron groups, and epididymides with noncontiguous ducts were excluded. In the fetal \*\*\*testis\*\*\*, exposure to linuron did not result in reduced mRNA expression of the AR or that of several steroidogenic enzymes, supporting the hypothesis that linuron does not reduce fetal \*\*\*testosterone\*\*\* prodn. Linuron induced a significant decrease in AR mRNA expression in GD 21 epididymides. Significant changes in mRNA expression in GD 21 and PND 7 epididymides were also identified in the epidermal growth factor (EGF), insulin-like growth factor 1 (IGF-1), bone morphogenetic protein (BMP), fibroblast growth factor (FGF), and Notch signaling pathways. These pathways are involved in tissue morphogenesis. Changes in the expression of AR and IGF-1 receptors were detected by immunostaining in malformed epididymides from linuron-exposed rats. Linuron induced changes in epididymal gene expression suggestive of altered paracrine interactions between the mesenchyme and epithelial cells during

development. The EGF, Notch, IGF-1, BMP4, and FGF signaling pathways may be involved in normal \*\*\*testosterone\*\*\* - mediated development of the Wolffian duct.  
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 59 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:461870 CAPLUS  
DN 139:174391  
TI Simultaneous gene clustering and subset selection for sample classification via MDL  
AU Joernsten, Rebecka; Yu, Bin  
CS Department of Statistics, Rutgers University, Piscataway, NJ, 08854, USA  
SO Bioinformatics (2003), 19(9), 1100-1109 CODEN: BOINFP; ISSN: 1367-4803  
PB Oxford University Press  
DT Journal  
LA English  
AB The microarray technol. allows for the simultaneous monitoring of thousands of genes for each sample. The high-dimensional gene expression data can be used to study similarities of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* across different samples to form a gene clustering. The clusters may be indicative of genetic pathways. Parallel to gene clustering is the important application of sample classification based on all or selected gene expressions. The gene clustering and sample classification are often undertaken sep., or in a directional manner (one as an aid for the other). However, such sepn. of these two tasks may occlude informative structure in the data. Here we present an algorithm for the simultaneous clustering of genes and subset selection of gene clusters for sample classification. We develop a new model selection criterion based on Rissanen's MDL (min. description length) principle. For the first time, an MDL code length is given for both explanatory variables (genes) and response variables (sample class labels). The final output of the proposed algorithm is a sparse and interpretable classification rule based on cluster centroids or the closest genes to the centroids. The algorithm for simultaneous gene clustering and subset selection for classification is applied to three publicly available data sets. For all three data sets, we obtain sparse and interpretable classification models based on centroids of clusters. At the same time, these models give competitive \*\*\*test\*\*\* error rates as the best reported methods. Compared with classification models based on single gene selections, our rules are stable in the sense that the no. of clusters has a small variability and the centroids of the clusters are well \*\*\*correlated\*\*\* (or consistent) across different cross validation samples. We also discuss models where the centroids of clusters are replaced with the genes closest to the centroids. These models show comparable \*\*\*test\*\*\* error rates to models based on single gene selection, but are more sparse as well as more stable. Moreover, we comment on how the inclusion of a classification criterion affects the gene clustering, bringing out class informative structure in the data.  
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 60 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:461867 CAPLUS  
DN 139:174388  
TI A statistical problem for inference to regulatory structure from associations of gene expression measurements with microarrays

AU Chu, Tianjiao; Glymour, Clark; Scheines, Richard; Spirtes, Peter  
CS Department of Philosophy, Carnegie Mellon University, FL, USA  
SO Bioinformatics (2003), 19(9), 1147-1152 CODEN: BOINFP; ISSN: 1367-4803  
PB Oxford University Press  
DT Journal  
LA English  
AB One approach to inferring genetic regulatory structure from microarray measurements of mRNA transcript hybridization is to est. the assocns. of gene expression levels measured in repeated samples. The assocns. may be estd. by. \*\*\*correlation\*\*\* coeffs. or by conditional frequencies (for discretized measurements) or by some other statistic. Although these procedures have been successfully applied to other areas, their validity when applied to microarray measurements has yet to be \*\*\*tested\*\*\*. This paper describes an elementary statistical difficulty for all such procedures, no matter whether based on Bayesian updating, conditional independence \*\*\*testing\*\*\*, or other machine learning procedures such as simulated annealing or neural net pruning. The difficulty obtains if a no. of cells from a common population are aggregated in a measurement of expression levels. Although there are special cases where the conditional assocns. are preserved under aggregation, in general inference of genetic regulatory structure based on conditional assocn. is unwarranted.  
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 61 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:431141 CAPLUS  
DN 139:80097  
TI human cancer-germline genes identified among 12 genes expressed in spermatogonia  
AU Lorient, Axelle; Boon, Thierry; De Smet, Charles  
CS Ludwig Institute for Cancer Research, Brussels Branch, and Cellular Genetics Unit, Universite Catholique de Louvain, Brussels, Belg.  
SO International Journal of Cancer (2003), 105(3), 371-376 CODEN: IJCNW; ISSN: 0020-7136  
PB Wiley-Liss, Inc.  
DT Journal  
LA English  
AB An important class of tumor-specific antigens is encoded by male germline-specific genes, such as MAGE genes, that are activated in many cancers of various histol. types as a result of the demethylation of their promoter region. A no. of these genes were shown to be expressed exclusively during the spermatogonia stage of spermatogenesis. A recent study reported the isolation of a new set of mouse genes that are expressed in spermatogonia but not in somatic tissues. Here, we \*\*\*tested\*\*\* the tumoral expression of the human orthologs of 12 of these genes. A remarkably high proportion, i.e., 5 of 12 genes, was found to be activated in a significant fraction of tumor samples of various histol. types. Expression levels of the 5 genes, namely, NXF2, TAF2Q, FTHL17, TDRD1 and TEX15, were evaluated in normal and tumoral tissues. Except for TEX15, these genes showed sufficiently high expression levels in tumors and low background transcription in normal somatic tissues to qualify them as genes that potentially code for tumor-specific antigens. Like previously described cancer-germline genes, the 5 genes were induced in cells treated with a demethylating agent.



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 62 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:424628 CAPLUS  
DN 139:208004  
TI Evaluation of hypothalamic gene expression in mice  
divergently selected for heat loss  
AU Wesolowski, Stephanie R.; Allan, Mark F.; Nielsen, Merlyn  
K.; Pomp, Daniel  
CS Department of Animal Science, University of Nebraska,  
Lincoln, NE, 68583-0908, USA  
SO Physiological Genomics (2003), 13(2), 129-137 CODEN:  
PHGEFP; ISSN: 1094-8341 URL:  
http://physiolgenomics.physiology.org/cgi/reprint/13/2/129.pdf  
PB American Physiological Society  
DT Journal; (online computer file)  
LA English

AB Mouse lines divergently selected for heat loss were  
evaluated for \*\*\*correlated\*\*\* responses in the hypothalamic  
transcriptome. High (MH) heat loss mice have .apprx.50%  
greater heat loss, .apprx.35% less body fat, .apprx.20% greater  
feed intake, .apprx.100% greater locomotor activity levels, and  
higher core body temp. compared with low (ML) heat loss mice.  
The authors evaluated hypothalamic expression between inbred  
lines derived from MH and ML lines (IH and IL, resp.) using cDNA  
microarrays and selected genes previously isolated in a large  
differential-display PCR expt. Northern anal. was used to confirm  
differences, revealing higher hypothalamic mRNA expression of  
oxytocin (Oxt) and tissue inhibitor of metalloproteinase 2 (timp-2)  
in the IH line. Real-time PCR \*\*\*assays\*\*\* were developed  
for Oxt, Timp-2, and ribosomal protein L3 (Rpl3, previously  
upregulated in IL) and confirmed differential expression of these  
genes with potential physiol. relevance in energy balance. These  
results provide information on \*\*\*correlated\*\*\* responses in  
the transcriptome of mice selected for high and low energy  
expenditure and reveal new information regarding genetic  
regulation of energy balance.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 63 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:421482 CAPLUS  
DN 138:380510  
TI Human nucleic acids differentially expressed in breast cancer  
and their uses for identification, assessment, prevention, and  
therapy of breast cancer  
IN Lillie, James; Xu, Yongyao; Wang, Youzhen; Steinmann,  
Kathleen  
PA Millennium Pharmaceuticals, Inc., USA  
SO U.S. Pat. Appl. Publ., 36 pp. CODEN: USXXCO  
DT Patent  
LA English

FAN.CNT 4	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			
PI	US 2003099974	A1	20030529	US 2002-198846
	20020718 US 2003099974	A1	20030529	US 2002-198846
	20020718			
PRAI	US 2001-306220P	P	20010718	US 2002-198846
A	20020718			

AB The invention relates to compns., kits, and methods for  
detecting, characterizing, preventing, and treating human breast  
cancers. Thus, 14,084 of newly identified nucleic acid markers

are provided, wherein changes in the levels of expression of one  
or more of the markers is \*\*\*correlated\*\*\* with the presence  
of breast cancer. Subtracted libraries are generated using a PCR-  
based method that allows the isolation of clones expressed at  
higher levels in one population of mRNA ( \*\*\*tester\*\*\* )  
compared to another population (driver). The technique results  
in both subtraction and normalization, which is an equalization of  
copy no. of low-abundance and high-abundance sequences. A  
group of 96 or more clones from each subtraction library is  
\*\*\*tested\*\*\* to confirm differential expression by reverse  
Southern hybridization. In addn., protein profiling expts. are  
undertaken to assess whether the proteins assocd. with the  
expression of individual markers of the invention are secreted.  
The markers are over- or under-expressed by .gtoreq.2-fold in at  
least 20% of stage 0 breast cancer patients, stage I breast  
cancer patients, stage IIA breast cancer patients, stage IIB  
breast cancer patients, stage IIIB breast cancer patients, stage  
IV breast cancer patients, grade I breast cancer patients, grade  
II breast cancer patients, grade III breast cancer patients,  
malignant breast cancer patients, ductal carcinoma breast cancer  
patients, and lobular carcinoma breast cancer patients. [This  
abstr. record is one of four records for this document  
necessitated by the large no. of index entries required to fully  
index the document and publication system constraints.].

L9 ANSWER 64 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:421481 CAPLUS  
DN 138:380509  
TI Human nucleic acids differentially expressed in breast cancer  
and their uses for identification, assessment, prevention, and  
therapy of breast cancer  
IN Lillie, James; Xu, Yongyao; Wang, Youzhen; Steinmann,  
Kathleen  
PA Millennium Pharmaceuticals, Inc., USA  
SO U.S. Pat. Appl. Publ., 36 pp. CODEN: USXXCO  
DT Patent  
LA English

FAN.CNT 4	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			
PI	US 2003099974	A1	20030529	US 2002-198846
	20020718 US 2003099974	A1	20030529	US 2002-198846
	20020718			
PRAI	US 2001-306220P	P	20010718	US 2002-198846
A	20020718			

AB The invention relates to compns., kits, and methods for  
detecting, characterizing, preventing, and treating human breast  
cancers. Thus, 14,084 of newly identified nucleic acid markers  
are provided, wherein changes in the levels of expression of one  
or more of the markers is \*\*\*correlated\*\*\* with the presence  
of breast cancer. Subtracted libraries are generated using a PCR-  
based method that allows the isolation of clones expressed at  
higher levels in one population of mRNA ( \*\*\*tester\*\*\* )  
compared to another population (driver). The technique results  
in both subtraction and normalization, which is an equalization of  
copy no. of low-abundance and high-abundance sequences. A  
group of 96 or more clones from each subtraction library is  
\*\*\*tested\*\*\* to confirm differential expression by reverse  
Southern hybridization. In addn., protein profiling expts. are  
undertaken to assess whether the proteins assocd. with the  
expression of individual markers of the invention are secreted.  
The markers are over- or under-expressed by .gtoreq.2-fold in at  
least 20% of stage 0 breast cancer patients, stage I breast  
cancer patients, stage IIA breast cancer patients, stage IIB  
breast cancer patients, stage IIIB breast cancer patients, stage  
IV breast cancer patients, grade I breast cancer patients, grade

II breast cancer patients, grade III breast cancer patients, malignant breast cancer patients, ductal carcinoma breast cancer patients, and lobular carcinoma breast cancer patients. [This abstr. record is one of four records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 65 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:421479 CAPLUS  
DN 138:380508

TI Human nucleic acids differentially expressed in breast cancer and their uses for identification, assessment, prevention, and therapy of breast cancer

IN Lillie, James; Xu, Yongyao; Wang, Youzhen; Steinmann, Kathleen

PA Millennium Pharmaceuticals, Inc., USA

SO U.S. Pat. Appl. Publ., 36 pp. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 4 PATENT NO.	KIND	DATE	APPLICATION
NO. DATE			
PI US 2003099974	A1	20030529	US 2002-198846
20020718 US 2003099974	A1	20030529	US 2002-198846
20020718			
PRAI US 2001-306220P	P	20010718	US 2002-198846
A 20020718			

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating human breast cancers. Thus, 14,084 of newly identified nucleic acid markers are provided, wherein changes in the levels of expression of one or more of the markers is \*\*\*correlated\*\*\* with the presence of breast cancer. Subtracted libraries are generated using a PCR-based method that allows the isolation of clones expressed at higher levels in one population of mRNA ( \*\*\*tester\*\*\* ) compared to another population (driver). The technique results in both subtraction and normalization, which is an equalization of copy no. of low-abundance and high-abundance sequences. A group of 96 or more clones from each subtraction library is \*\*\*tested\*\*\* to confirm differential expression by reverse Southern hybridization. In addn., protein profiling expts. are undertaken to assess whether the proteins assocd. with the expression of individual markers of the invention are secreted. The markers are over- or under-expressed by .gtoreq.2-fold in at least 20% of stage 0 breast cancer patients, stage I breast cancer patients, stage IIA breast cancer patients, stage IIB breast cancer patients, stage IIIB breast cancer patients, stage IV breast cancer patients, grade I breast cancer patients, grade II breast cancer patients, grade III breast cancer patients, malignant breast cancer patients, ductal carcinoma breast cancer patients, and lobular carcinoma breast cancer patients. [This abstr. record is one of four records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 66 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:417868 CAPLUS  
DN 138:398390

TI Fractionation of Escherichia coli cell populations at different stages during growth transition to stationary phase by Percoll density gradient centrifugation

IN Ishihama, Akira

PA Japan Science and Technology Corporation, Japan

SO PCT Int. Appl., 29 pp. CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1 PATENT NO.	KIND	DATE	APPLICATION
NO. DATE			
PI WO 2003044180	A1	20030530	WO 2002-JP4718
20020515 W: CA, RU, US			RW: DE, DK, ES, FR, GB, IT, NL,
SE JP 2003159050	A2	20030603	JP 2001-356118
20011121			
PRAI JP 2001-356118	A	20011121	

AB A method of sepg. unicellular microorganisms based on difference in cell cycle/differentiation stages, is disclosed. Sepg. and fractionating unicellular microorganisms such as bacteria depending on difference in the cell cycle/differentiation states \*\*\*correlated\*\*\* with expression level of genes expressed in each state. Thus, it was found that unicellular microorganisms can be sepd. depending on difference in cell cycle/differentiation stages by Percoll d. gradient centrifugation. Accordingly, comprehensive \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* can be analyzed with the use of a homogeneous cell mass. Cultures of Escherichia coli could be sepd. into more than 15 cell populations, each forming a discrete band after Percoll gradient centrifugation. The cell sepn. was found to result from the difference in buoyant d. but not the size difference. The cell d. increases upon transition from exponential growth to stationary phase. Exponential phase cultures formed at least five discrete bands with lower densities, whereas stationary phase cultures formed more than 10 bands with higher densities. Two mol. markers characterizing each cell population were identified: the functioning promoter species, as identified by measuring the expression of green fluorescent protein under the control of \*\*\*test\*\*\* promoters; and the expressed protein species, as monitored by quant. immunoblotting. These findings suggest that the growth phase-coupled transition of E. coli phenotype is discontinuous.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 67 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:413965 CAPLUS  
DN 138:380507

TI Human nucleic acids differentially expressed in breast cancer and their uses for identification, assessment, prevention, and therapy of breast cancer

IN Lillie, James; Xu, Yongyao; Wang, Youzhen; Steinmann, Kathleen

PA Millennium Pharmaceuticals, Inc., USA

SO U.S. Pat. Appl. Publ., 36 pp. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 4 PATENT NO.	KIND	DATE	APPLICATION
NO. DATE			
PI US 2003099974	A1	20030529	US 2002-198846
20020718 US 2003099974	A1	20030529	US 2002-198846
20020718 US 2003099974	A1	20030529	US 2002-198846
20020718			
US 2002-198846			
20020718 US 2003099974	A1	20030529	US 2002-198846
20020718			
PRAI US 2001-306220P	P	20010718	US 2002-198846
A 20020718			

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating human breast cancers. Thus, 14,084 of newly identified nucleic acid markers are provided, wherein changes in the levels of expression of one or more of the markers is \*\*\*correlated\*\*\* with the presence of breast cancer. Subtracted libraries are generated using a PCR-based method that allows the isolation of clones expressed at

higher levels in one population of mRNA ( **\*\*\*tester\*\*\*** ) compared to another population (driver). The technique results in both subtraction and normalization, which is an equalization of copy no. of low-abundance and high-abundance sequences. A group of 96 or more clones from each subtraction library is **\*\*\*tested\*\*\*** to confirm differential expression by reverse Southern hybridization. In addn., protein profiling expts. are undertaken to assess whether the proteins assocd. with the expression of individual markers of the invention are secreted. The markers are over- or under-expressed by .gtoreq.2-fold in at least 20% of stage 0 breast cancer patients, stage I breast cancer patients, stage IIA breast cancer patients, stage IIB breast cancer patients, stage IIIB breast cancer patients, stage IV breast cancer patients, grade I breast cancer patients, grade II breast cancer patients, grade III breast cancer patients, malignant breast cancer patients, ductal carcinoma breast cancer patients, and lobular carcinoma breast cancer patients. [This abstr. record is one of four records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 68 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:404400 CAPLUS  
DN 139:256489

TI Effects of Minimally Toxic Levels of Carbonyl Cyanide P-(Trifluoromethoxy) Phenylhydrazone (FCCP), Elucidated through Differential Gene Expression with Biochemical and Morphological **\*\*\*Correlations\*\*\***

AU Kuruvilla, Sabu; Qualls, Charles W., Jr.; Tyler, Ronald D.; Witherspoon, Sam M.; Benavides, Gina R.; Yoon, Lawrence W.; Dold, Karen; Brown, Roger H.; Sangiah, Subbiah; Morgan, Kevin T.

CS Oklahoma State University, Stillwater, OK, 74078, USA  
SO Toxicological Sciences (2003), 73(2), 348-361 CODEN: TOSCF2; ISSN: 1096-6080

PB Oxford University Press

DT Journal

LA English

AB Uncouplers of oxidative phosphorylation have relevance to bioenergetics and obesity. The mechanisms of action of chem. uncouplers of oxidative phosphorylation on biol. systems were evaluated using differential gene expression. The transcriptional response in human rhabdomyosarcoma cell line (RD), was elucidated following treatment with carbonyl cyanide p-(trifluoromethoxy) phenylhydrazone (FCCP), a classical uncoupling agent. Changes in mitochondrial membrane potential were used as the biol. dosimeter. There was an increase in membrane depolarization with increasing concns. of FCCP. The concn. at 75% uncoupling (20 .mu.M) was chosen to study gene expression changes, using cDNA-based large-scale differential gene expression (LSDGE) platforms. At the above concn., subtle light microscopic and clear gene expression changes were obsd. at 1, 2, and 10 h. Statistically significant transcriptional changes were largely assocd. with protein synthesis, cell cycle regulation, cytoskeletal proteins, energy metab., apoptosis, and inflammatory mediators. Bromodeoxyuridine (BrdU) and propidium iodide (PI) **\*\*\*assays\*\*\*** revealed cell cycle arrest to occur in the G1 and S phases. There was a significant initial decrease in the intracellular ATP concns. The following seven genes were selected as potential mol. markers for chem. uncouplers: seryl-tRNA synthetase (Ser-tRS), glutamine-hydrolyzing asparagine synthetase (Glut-HAS), mitochondrial bifunctional methylenetetrahydrofolate dehydrogenase (Mit BMD), mitochondrial heat shock 10-kDa protein (Mit HSP 10), proliferating cyclic nuclear antigen (PCNA), cytoplasmic beta-actin (Act B), and growth arrest and DNA damage-inducible protein

153 (GADD153). Transcriptional changes of all seven genes were later confirmed with reverse transcription-polymerase chain reaction (RT-PCR). These results suggest that gene expression changes may provide a sensitive indicator of uncoupling in response to chem. exposure.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 69 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:404306 CAPLUS  
DN 139:144496

TI Inference of transcriptional regulation relationships from gene expression data

AU Kwon, Andrew T.; Hoos, Holger H.; Ng, Raymond  
CS Department of Computer Science, University of British Columbia, Vancouver, BC, Can.

SO Bioinformatics (2003), 19(8), 905-912 CODEN: BOINFP; ISSN: 1367-4803

PB Oxford University Press

DT Journal

LA English

AB In order to find gene regulatory networks from microarray data, it is important to first find direct regulatory relationships between pairs of genes. We propose a new method for finding potential regulatory relationships between pairs of genes from microarray time series data and apply it to expression data for cell-cycle related genes in yeast. We compare our algorithm, dubbed the event method, with the earlier **\*\*\*correlation\*\*\*** method and the edge detection method by Filkov et al. When **\*\*\*tested\*\*\*** on known transcriptional regulation genes, all three methods are able to find similar nos. of true positives. The results indicate that our algorithm is able to identify true pos. pairs that are different from those found by the two other methods. We also compare the **\*\*\*correlation\*\*\*** and the event methods using synthetic data and find that typically, the event method obtains better results.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 70 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:398105 CAPLUS  
DN 139:345477

TI A Rational Approach to Personalized Anticancer Therapy: Chemoinformatic Analysis Reveals Mechanistic Gene-Drug Associations

AU Shedden, Kerby; Townsend, Leroy B.; Drach, John C.; Rosania, Gustavo R.

CS Department of Statistics, The University of Michigan, Ann Arbor, MI, 48109, USA

SO Pharmaceutical Research (2003), 20(6), 843-847 CODEN: PHREEB; ISSN: 0724-8741

PB Kluwer Academic/Plenum Publishers

DT Journal

LA English

AB To predict the response of cells to chemotherapeutic agents based on **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** **\*\*\*profiles\*\*\***, we performed a chemoinformatic study of a set of std. anticancer agents **\*\*\*assayed\*\*\*** for activity against a panel of 60 human tumor-derived cell lines from the Developmental Therapeutics Program (DTP) at the National Cancer Institute (NCI). Mechanistically-relevant gene:drug activity assocns. were identified in the scientific literature. The **\*\*\*correlations\*\*\*** between expression levels of drug target genes and the activity of the drugs against the NCI's 60 cell line panel were calcd.

across and within each tumor tissue type, using published drug activity and gene expression data. Compared to other mechanistically-relevant gene-drug assocns., that of tritiribine phosphate (TCN-P) and adenosine kinase (ADK) was exceptionally strong-overall and within tumor tissue types-across the 60 cell lines \*\*\*profiled\*\*\* for chemosensitivity (1) and \*\*\*gene\*\*\* \*\*\*expression\*\*\* (2). The results suggest ADK expression may be useful for stratifying TCN-P-responsive vs. non-responsive tumors. Based on TCN-P's mechanism of action and the obsd. TCN-P:ADK assocn., we contend that catalytic drug activation provides a rational, mechanistic basis for personalizing cancer treatment based on tumor-specific differences in the expression of drug-activating enzymes.  
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 71 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:396364 CAPLUS DN 138:381662

TI Precipitation of metallic compound in method and apparatus for the identification and/or the quantification of a target compound obtained from a biological sample upon chips IN Remacle, Jose; Demarteau, Joseph PA Belg.

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 574,626. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3	PATENT NO.	KIND	DATE	APPLICATION NO.
PI	US 2003096321	A1	20030522	US 2002-189288
	20020701 EP 1054259	A1	20001122	EP 1999-870106
	19990519 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		US 2003124522	
A1	20030703 US 2000-574626		20000519	
PRAI	EP 1999-870106	A	19990519	EP 2000-870025
A	20000218 US 2000-574626	A2	20000519	

AB The present invention is related to a method for the identification and/or the quantification of a target compd. obtained from a sample, preferably a biol. sample, comprising the steps of putting into contact the target compd. with a capture mol. in order to allow a specific binding between said target compd. with a capture mol., said capture mol. being fixed upon a surface of a solid support according to an array comprising a d. of at least 20 discrete regions per cm<sup>2</sup>, each of said discrete regions being fixed with one species of capture mols., performing a reaction leading to a ppt. formed at the location of said binding, detg. the possible presence of ppt.(s) in discrete region(s), and \*\*\*correlating\*\*\* the presence of the ppt.(s) at the discrete region(s) with the identification and/or a quantification of said target compd. Silver enhancement was used in detection of DNA or proteins on biochips, in microarray anal. of gene expression of livers of phenobarbital-treated rats, and in detection of IgE and human autoimmune antibodies.

L9 ANSWER 72 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:389249 CAPLUS DN 140:124607

TI Computational analyses of high-throughput protein-protein interaction data

AU Chen, Yu; Xu, Dong

CS Protein Informatics Group, Life Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN, 37830, USA

SO Current Protein and Peptide Science (2003), 4(3), 159-180 CODEN: CPPSCM; ISSN: 1389-2037

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. Protein-protein interactions play important roles in nearly all events that take place in a cell. High-throughput exptl. techniques enable the study of protein-protein interactions at the proteome scale through systematic identification of phys. interactions among all proteins in an organism. High-throughput protein-protein interaction data, with ever-increasing vol., are becoming the foundation for new biol. discoveries. A great challenge to bioinformatics is to manage, analyze, and model these data. In this review, we describe several databases that store, query, and visualize protein-protein interaction data. Comparison between exptl. techniques shows that each high-throughput technique such as yeast two-hybrid \*\*\*assay\*\*\* or protein complex identification through mass spectrometry has its limitations in detecting certain types of interactions and they are complementary to each other. In silico methods using protein/DNA sequences, domain and structure information to predict protein-protein interaction can expand the scope of exptl. data and increase the confidence of certain protein-protein interaction pairs. Protein-protein interaction data \*\*\*correlate\*\*\* with other types of data, including protein function, subcellular location, and \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\*. Highly connected proteins are more likely to be essential based on the analyses of the global architecture of large-scale interaction network in yeast. Use of protein-protein interaction networks, preferably in conjunction with other types of data, allows assignment of cellular functions to novel proteins and derivation of new biol. pathways. As demonstrated in our study on the yeast signal transduction pathway for amino acid transport, integration of high-throughput data with traditional biol. resources can transform the protein-protein interaction data from noisy information into knowledge of cellular mechanisms.  
RE.CNT 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 73 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:375496 CAPLUS DN 139:194927

TI Gene microarrays in hippocampal aging: Statistical profiling identifies novel processes \*\*\*correlated\*\*\* with cognitive impairment

AU Blalock, Eric M.; Chen, Kuey-Chu; Sharrow, Keith; Herman, James P.; Porter, Nada M.; Foster, Thomas C.; Landfield, Philip W.

CS Department of Molecular and Biomedical Pharmacology, University of Kentucky College of Medicine, Lexington, KY, 40536-0298, USA

SO Journal of Neuroscience (2003), 23(9), 3807-3819 CODEN: JNRSDS; ISSN: 0270-6474

PB Society for Neuroscience

DT Journal

LA English

AB Gene expression microarrays provide a powerful new tool for studying complex processes such as brain aging. However, inferences from microarray data are often hindered by multiple comparisons, small sample sizes, and uncertain relationships to functional endpoints. Here we sought gene expression \*\*\*correlates\*\*\* of aging-dependent cognitive decline, using statistical profiling of gene microarrays in well powered groups of young, mid-aged, and aged rats (n = 10 per group). Animals

were trained on two memory tasks, and the hippocampal CA1 region of each was analyzed on an individual microarray (one chip per animal). Aging- and cognition-related genes were identified by \*\*\*testing\*\*\* each gene by ANOVA (for aging effects) and then by Pearson's \*\*\*test\*\*\* (\*\*\*correlating\*\*\* expression with memory). Genes identified by this algorithm were assocd. with several phenomena known to be aging-dependent, including inflammation, oxidative stress, altered protein processing, and decreased mitochondrial function, but also with multiple processes not previously linked to functional brain aging. These novel processes included downregulated early response signaling, biosynthesis and activity-regulated synaptogenesis, and upregulated myelin turnover, cholesterol synthesis, lipid and monoamine metab., iron utilization, structural reorganization, and intracellular Ca2+ release pathways. Multiple transcriptional regulators and cytokines also were identified. Although most gene expression changes began by mid-life, cognition was not clearly impaired until late life. Collectively, these results suggest a new integrative model of brain aging in which genomic alterations in early adulthood initiate interacting cascades of decreased signaling and synaptic plasticity in neurons, extracellular changes, and increased myelin turnover-fueled inflammation in glia that cumulatively induce aging-related cognitive impairment.

RE.CNT 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 74 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:375413 CAPLUS  
DN 139:116926  
TI MetNet: Software to build and model the biogenetic lattice of arabidopsis  
AU Wurtele, Eve Syrkin; Li, Jie; Diao, Lixia; Zhang, Hailong; Foster, Carol M.; Fatland, Beth; Dickerson, Julie; Brown, Andrew; Cox, Zach; Cook, Dianne; Lee, Eun-Kyung; Hofmann, Heike  
CS Department of Genetics, Cellular and Developmental Biology, Iowa State University, Ames, IA, 50011, USA  
SO Comparative and Functional Genomics (2003), 4(2), 239-245  
CODEN: CFGOAT; ISSN: 1531-6912  
PB John Wiley & Sons Ltd.  
DT Journal  
LA English  
AB MetNet  
(<http://www.botany.iastate.edu/apprx.mash/metnetex/metabolic.netex.html>) is publicly available software in development for anal. of genome-wide RNA, protein and metabolite profiling data. The software is designed to enable the biologist to visualize, statistically analyze and model a metabolic and regulatory network map of Arabidopsis, combined with \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* data. It contains a JAVA interface to an interactions database (MetNetDB) contg. information on regulatory and metabolic interactions derived from a combination of web databases (TAIR, KEGG, BRENDA) and input from biologists in their area of expertise. FCModeler captures input from MetNetDB in a graphical form. Sub-networks can be identified and interpreted using simple fuzzy cognitive maps. FCModeler is intended to develop and evaluate hypotheses, and provide a modeling framework for assessing the large amts. of data captured by high-throughput gene expression expts. FCModeler and MetNetDB are currently being extended to three-dimensional virtual reality display. The MetNet map, together with gene expression data, can be viewed using multivariate graphics tools in GGobi linked with the data analytic tools in R. Users can highlight different parts of the metabolic network and see the relevant expression data highlighted in other

data plots. Multi-dimensional expression data can be rotated through different dimensions. Statistical anal. can be computed alongside the visual. MetNet is designed to provide a framework for the formulation of \*\*\*testable\*\*\* hypotheses regarding the function of specific genes, and in the long term provide the basis for identification of metabolic and regulatory networks that control plant compri. and development.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 75 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:362335 CAPLUS  
DN 139:82977  
TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of hepatoma cell line HLE  
AU Liu, Lian-Xin; Liu, Zhi-Hua; Jiang, Hong-Chi; Zhang, Wei-Hui; Qi, Shu-Yi; Hu, Jie; Wang, Xiu-Qin; Wu, Min  
CS Department of Surgery, First Clinical College, Harbin Medical University, Harbin, Heilongjiang Province, 150001, Peop. Rep. China  
SO World Journal of Gastroenterology (2003), 9(4), 683-687  
CODEN: WJGAF2; ISSN: 1007-9327  
PB World Journal of Gastroenterology  
DT Journal  
LA English  
AB AIM: To investigate the global gene expression of cancer related genes in hepatoma cell line HLE using Atlas Human Cancer Array membranes with 588 well-characterized human genes related with cancer and tumor biol. METHODS: Hybridization of cDNA blotting membrane was performed with 32P-labeled cDNA probes synthesized from RNA isolated from Human hepatoma cell line HLE and non-cirrhotic normal liver which was liver transplantation donor. AtlasImage, a software specific to array, was used to analyze the result. The expression pattern of some genes identified by Atlas arrays hybridization was confirmed by reverse transcription polymerase chain reaction (RT-PCR) in 24 pairs of specimens and Northern blot of 4 pairs of specimens. RESULTS: The differential expression of cell cycle/growth regulator in hepatocellular carcinoma (HCC) showed a stronger tendency toward cell proliferation with more than 1.5-fold up-regulation of Cyclin C, ERK5, ERK6, E2F-3, TFDP-2 and CK4. The anti-apoptotic factors such as Akt-1 were up-regulated, whereas the promotive genes of apoptosis such as ABL2 were down-regulated. Among oncogene/tumors suppressors, SKY was down-regulated. Some genes such as Integrin beta 8, Integrin beta 7, DNA-PK, CSPCP, byglycan, Tenacin and DNA Topo were up-regulated. A no. of genes, including LAR, MEK1, eps15, TDGF1, ARHGDIA were down-regulated. In general, expression of the cancer progression genes was up-regulated, while expression of anti-cancer progression genes was down-regulated. These differentially expressed genes \*\*\*tested\*\*\* with RT-PCR were in consistent with cDNA array findings. CONCLUSION: Investigation of these genes in HCC is helpful in disclosing mol. mechanism of pathogenesis and progression of HCC. For the first time few genes were discovered in HCC. Further study is required for the precise relationship between the altered genes and their \*\*\*correlation\*\*\* with the pathogenesis of HCC.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 76 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:356698 CAPLUS  
DN 138:349688

TI Use of Chi square \*\*\*tests\*\*\* for analysis of  
\*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* obtained  
by microarray technology

IN Bader, Joel S.

PA Curagen Corporation, USA

SO PCT Int. Appl., 58 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	----	-----	-----

PI WO 2003038432 A1 20030508 WO 2002-US22450  
20020715 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,  
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,  
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,  
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ,  
SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,  
GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI,  
CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2003105595  
A1 20030605 US 2002-196674 20020715  
PRAI US 2001-305482P P 20010713

AB The present invention relates to systems and methods that  
utilize statistical means for analyzing expression of biol. samples.  
Statistical concepts employed include population detns., normal  
distributions, \*\*\*correlations\*\*\* between related measures;  
parameters utilized, Chi Square anal., degrees of freedom, mean,  
variance and std. deviations from the mean.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR  
THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 77 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:353159 CAPLUS  
DN 139:147398

TI Classification of Follicular Thyroid Tumors by Molecular  
Signature: Results of Gene Profiling

AU Barden, Catherine B.; Shister, Katherine W.; Zhu, Baixin;  
Guiter, Gerardo; Greenblatt, David Y.; Zeiger, Martha A.; Fahey,  
Thomas J., III

CS Departments of Surgery and Pathology, New York  
Presbyterian Hospital and Weill Medical College of Cornell  
University, New York, NY, 10021, USA

SO Clinical Cancer Research (2003), 9(5), 1792-1800 CODEN:  
CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB PURPOSE: Thyroid nodules are common, with a lifetime risk  
of developing a clin. significant thyroid nodule of 10% or higher.  
Preoperative diagnosis was greatly enhanced by the introduction  
of fine needle aspiration in the 1970s, but there has been little  
advancement since that time. Discrimination between benign and  
malignant follicular neoplasms is currently not possible by fine  
needle aspiration and can even be difficult after full pathol.  
review. The purpose of these studies is to identify genes  
expressed in follicular adenomas and carcinomas of the thyroid  
that will permit mol. differentiation of these neoplasms. Exptl.  
Design: \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\*  
of 17 thyroid follicular tumors were analyzed by oligonucleotide  
array anal. Gene profiles for follicular adenomas and carcinomas  
were identified, and the two groups were compared for  
differences in expression levels. The differentially expressed

genes were used to perform a hierarchical clustering anal.  
training set. Five follicular tumors with diagnosis undisclosed to  
the investigators and 2 minimally invasive carcinomas were  
entered into the cluster anal. as a \*\*\*test\*\*\* set to det.  
whether diagnosis by gene profile \*\*\*correlated\*\*\* with that  
obtained by pathol. evaluation. RESULTS: Thyroid follicular  
adenomas and carcinomas showed strikingly distinct  
\*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\*. The  
expression patterns of 105 genes were significantly different  
between follicular adenoma and carcinoma. Many  
uncharacterized genes contributed to the distinction between  
tumor types. For five follicular tumors for which the final  
diagnosis was undisclosed, the clustering algorithm gave the  
correct diagnosis in all 5 cases. CONCLUSIONS: Gene profiling is  
a useful tool to predict the mol. diagnosis of follicular thyroid  
tumors. Genes were identified that reliably differentiate follicular  
thyroid carcinoma from adenoma. This study provides insight  
into genes that may be important in the mol. pathogenesis of  
follicular thyroid tumors, as well candidates for preoperative  
diagnosis of follicular thyroid carcinoma.  
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 78 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:333416 CAPLUS  
DN 139:34649

TI Functional analysis of an arthritogenic synovial fibroblast

AU Aidinis, Vasilis; Plows, David; Haralambous, Sylva; Armaka,  
Maria; Papadopoulos, Petros; Kanaki, Maria; Koczan,  
Dirk; Thiesen, Hans Juergen; Kollias, George

CS Institute of Immunology, Biomedical Sciences Research  
Center 'Alexander Fleming', Athens, Greece

SO Arthritis Research & Therapy (2003), 5(3), R140-R157  
CODEN: ARTRCV; ISSN: 1478-6362 URL: <http://arthritis-research.com/content/pdf/ar749.pdf>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Increasing attention was directed towards identifying non-T-  
cell mechanisms as potential therapeutic targets in rheumatoid  
arthritis. Synovial fibroblast (SF) activation, a hallmark of  
rheumatoid arthritis, results in inappropriate prodn. of  
chemokines and matrix components, which in turn lead to bone  
and cartilage destruction. We have demonstrated that SFs have  
an autonomous pathogenic role in the development of the  
disease, by showing that they have the capacity to migrate  
throughout the body and cause pathol. specifically to the joints.  
In order to decipher the pathogenic mechanisms that govern SF  
activation and pathogenic potential, the authors used the 2 most  
prominent methods of differential gene expression anal.,  
differential display and DNA microarrays, in a search for  
deregulated cellular pathways in the arthritogenic SF. Functional  
clustering of differentially expressed genes, validated by  
dedicated in vitro functional \*\*\*assays\*\*\*, implicated a no. of  
cellular pathways in SF activation. Among them, diminished  
adhesion to the extracellular matrix was shown to  
\*\*\*correlate\*\*\* with increased proliferation and migration to  
this matrix. These findings support an aggressive role for the SF  
in the development of the disease and reinforce the perspective  
of a transformed-like character of the SF.

RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 79 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN



AN 2003:327376 CAPLUS  
DN 139:63908  
TI \*\*\*Testing\*\*\* for differentially expressed genes with microarray data  
AU Tsai, Chen-An; Chen, Yi-Ju; Chen, James J.  
CS Division of Biometry and Risk Assessment, National Center for Toxicological Research, Food and Drug Administration, Jefferson, AR, 72079, USA  
SO Nucleic Acids Research (2003), 31(9), e52/1-e52/10 CODEN: NARHAD; ISSN: 0305-1048  
PB Oxford University Press  
DT Journal  
LA English  
AB This paper compares the type I error and power of the one- and two-sample t- \*\*\*tests\*\*\*, and the one- and two-sample permutation \*\*\*tests\*\*\* for detecting differences in gene expression between two microarray samples with replicates using Monte Carlo simulations. When data are generated from a normal distribution, type I errors and powers of the one-sample parametric t- \*\*\*test\*\*\* and one-sample permutation \*\*\*test\*\*\* are very close, as are the two-sample t- \*\*\*test\*\*\* and two-sample permutation \*\*\*test\*\*\*, provided that the no. of replicates is adequate. When data are generated from a t-distribution, the permutation \*\*\*tests\*\*\* outperform the corresponding parametric \*\*\*tests\*\*\* if the no. of replicates is at least five. For data from a two-color dye swap expt., the one-sample \*\*\*test\*\*\* appears to perform better than the two-sample \*\*\*test\*\*\* since expression measurements for control and treatment samples from the same spot are \*\*\*correlated\*\*\*. For data from independent samples, such as the one-channel array or two-channel array expt. using ref. design, the two-sample t- \*\*\*tests\*\*\* appear more powerful than the one-sample t- \*\*\*tests\*\*\*.  
RE.CNT .19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 80 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:311929 CAPLUS  
DN 139:82902  
TI Using Gene Expression Ratios to Predict Outcome Among Patients With Mesothelioma  
AU Gordon, Gavin J.; Jensen, Roderick V.; Hsiao, Li-Li; Gullans, Steven R.; Blumenstock, Joshua E.; Richards, William G.; Jaklitsch, Michael T.; Sugarbaker, David J.; Bueno, Raphael  
CS Division Thoracic Surgery, Brigham and Womens Hospital, Harvard Medical School, Boston, MA, USA  
SO Journal of the National Cancer Institute (2003), 95(8), 598-605 CODEN: JNCIEQ; ISSN: 0027-8874  
PB Oxford University Press  
DT Journal  
LA English  
AB We have recently demonstrated that simple ratios of the expression levels of selected genes in tumor samples can be used to distinguish among types of thoracic malignancies. We examd. whether this technique could predict treatment-related outcome for patients with mesothelioma. We used \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* data previously collected from 17 mesothelioma patients with different overall survival times to define 2 outcome-related groups of patients and to train an expression ratio-based outcome predictor model. A Student's t \*\*\*test\*\*\* was used to identify genes among the 2 outcome groups that had statistically significant, inversely \*\*\*correlated\*\*\* expression levels; those genes were used to form prognostic expression ratios. We used a combination of several highly accurate expression ratios and cross-validation

techniques to assess the internal consistency of this predictor model, quant. reverse transcription-polymerase chain reaction of tumor RNA to confirm the microarray data, and Kaplan-Meier survival anal. to validate the model among an independent set of 29 mesothelioma tumors. All statistical \*\*\*tests\*\*\* were 2-sided. We developed an expression ratio-based \*\*\*test\*\*\* capable of identifying 100% (17/17) of the samples used to train the model. This \*\*\*test\*\*\* remained highly accurate (88%, 15/17) after cross-validation. A 4-gene expression ratio \*\*\*test\*\*\* statistically significantly (P = .0035) predicted treatment-related patient outcome in mesothelioma independent of the histol. subtype of the tumor. Gene expression ratio-based anal. accurately predicts treatment-related outcome in mesothelioma samples. This technique could impact the clin. treatment of mesothelioma by allowing the preoperative identification of patients with widely divergent prognoses.  
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 81 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:300516 CAPLUS  
DN 138:297598  
TI Analysis of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* in disease tissues in the determination of sensitivity or resistance to chemotherapeutics  
IN Tamayo, Pablo; Staunton, Jane E.; Slonim, Donna K.; Collier, Hilary A.; Golub, Todd R.; Lander, Eric S.; Mesirov, Jill P.  
PA USA  
SO U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U.S. Ser. No. 544,627. CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION  
NO. DATE -----  
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PI US 2003073083 A1 20030417 US 2001-968627  
20011001 US 6647341 B1 20031111 US 2000-544627  
20000406 US 2003017481 A1 20030123 US 2002-74789  
20020212  
PRAI US 1999-128664P P 19990409 US 1999-135397P  
P 19990521 US 1999-158467P P 19991008 US  
1999-159477P P 19991014 US 2000-188765P P  
20000313 US 2000-544627 A2 20000406 US 2000-  
236769P P 20000929  
AB Methods and app. for identifying genes that can be used to classify or to predict classes for samples based on \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* are described. These methods and app. may be used to discover new, previously unknown classes based on their \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. Methods, computer systems and app. for classifying or predicting whether a diseased tissue sample will be sensitive or resistant to chem. treatment are described. Classification occurs based on anal. of gene expression data from samples that have been subjected to one or more compds. \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* were analyzed in tumor cells that had been identified unambiguously by classical diagnostic methods. Sets of 50 genes that distinguished normal and neoplastic tissue were identified by microarray hybridization and \*\*\*tested\*\*\* for their ability to identify neoplastic cell samples. These sets of genes were 100% accurate in identifying neoplastic tissues. Clusters that could be used to differentiate acute myelogenous leukemia from acute lymphoblastic leukemia were identified.

L9 ANSWER 82 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:297366 CAPLUS

DN 139:177684

TI Microarray Analysis Using Amplified mRNA from Laser Capture Microdissection of Microscopic Hepatocellular Precancerous Lesions and Frozen Hepatocellular Carcinomas Reveals Unique and Consistent \*\*\*Gene\*\*\*

\*\*\*Expression\*\*\* \*\*\*Profiles\*\*\*

AU Yim, Sun Hee; Ward, Jerrold M.; Dragan, Yvonne; Yamada, Atsushi; Scacheri, Peter C.; Kimura, Shioko; Gonzalez, Frank J.

CS National Cancer Institute, Center for Cancer Research, Laboratory of Metabolism, NIH, Bethesda, MD, 20892, USA

SO Toxicologic Pathology (2003), 31(3), 295-303 CODEN: TOPADD; ISSN: 0192-6233

PB Taylor & Francis, Inc.

DT Journal

LA English

AB The indirect labeling cDNA microarray technique was used to evaluate \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of pure cell populations from frozen sections of carcinomas and adenomas harvested from precancerous hepatocellular lesions by laser capture microdissection (LCM). The levels of differentially expressed genes were investigated using a cDNA microarray with 9,984 features with only 2 ug of 2-round amplified aRNA, equiv. to 35 cells from LCM-adenomas and frozen samples of carcinomas from simian virus 40 (SV40) large T antigen transgenic rats. A total of 855 genes were identified as being 3-fold or more differentially expressed in carcinomas or adenomas as compared to normal tissue controls. Among these 855 genes, 71 genes were differentially expressed in both carcinomas and adenomas. Commonly up-regulated genes in both carcinoma and adenomas were 28 while 41 of the 71 genes were commonly down-regulated. Two genes, Igh1 (Ig heavy chain 1(Serum IgG2a), Image clone ID: 875880) and EST clone (AI893585, Image clone ID: 596604) were more than 7-fold up-regulated in carcinomas and 6-fold down-regulated in adenomas. In Cy5 and Cy3 reciprocal expts. for screening out false pos. signals, the amplified carcinomas showed higher Pearson \*\*\*Correlation\*\*\* Coeff. values (-0.94 and -0.92) than the LCM-amplified adenoma samples (-0.79 and -0.84). LCM-amplified samples provided higher signal intensities over backgrounds and a greater av. of Cy5: Cy3 ratios. Expression levels of mRNAs from selected genes, detd. by traditional dot blot anal., revealed that 36 of 40 \*\*\*tested\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* were consistent with the microarray data. Thus, amplified aRNA harvested from homogeneous cell types using LCM can be applied to study \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* by microarray anal.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 83 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:290584 CAPLUS

DN 139:522

TI \*\*\*Expression\*\*\* \*\*\*profiling\*\*\* of blood samples from an SU5416 phase II metastatic colorectal cancer clinical trial: a novel strategy for biomarker identification

AU DePrimo, Samuel E.; Wong, Lily M.; Khatry, Deepak B.; Nicholas, Susan L.; Manning, William C.; Smolich, Beverly D.; O'Farrell, Anne-Marie; Cherrington, Julie M.

CS Preclinical Res. Exploratory Development, SUGEN, Inc., South San Francisco, CA, 94080, USA

SO BMC Cancer (2003), 3, No pp. given CODEN: BCMACL; ISSN: 1471-2407 URL: <http://www.biomedcentral.com/1471-2407/3/3>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Microarray-based \*\*\*gene\*\*\* \*\*\*expression\*\*\*

\*\*\*profiling\*\*\* is a powerful approach for the identification of mol. biomarkers of disease, particularly in human cancers. Utility of this approach to measure responses to therapy is less well established, in part due to challenges in obtaining serial biopsies. Identification of suitable surrogate tissues will help minimize limitations imposed by those challenges. This study describes an approach used to identify gene expression changes that might serve as surrogate biomarkers of drug activity.

\*\*\*Expression\*\*\* \*\*\*profiling\*\*\* using microarrays was applied to peripheral blood mononuclear cell (PBMC) samples obtained from patients with advanced colorectal cancer participating in a Phase III clin. trial. The PBMC samples were harvested pre-treatment and at the end of the first 6-wk cycle from patients receiving std. of care chemotherapy or std. of care plus SU5416, a vascular endothelial growth factor (VEGF) receptor tyrosine kinase (RTK) inhibitor. Results from matched pairs of PBMC samples from 23 patients were queried for expression changes that consistently \*\*\*correlated\*\*\* with SU5416 administration. Thirteen transcripts met this selection criterion; six were further \*\*\*tested\*\*\* by quant. RT-PCR anal. of 62 addnl. samples from this trial and a second SU5416 Phase III trial of similar design. This method confirmed four of these transcripts (CD24, lactoferrin, lipocalin 2, and MMP-9) as potential biomarkers of drug treatment. Discriminant anal. showed that \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of these 4 transcripts could be used to classify patients by treatment arm in a predictive fashion. In conclusions, these results establish a foundation for the further exploration of peripheral blood cells as a surrogate system for biomarker analyses in clin. oncol. studies. RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 84 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:278858 CAPLUS

DN 138:266969

TI Gene expression profiles useful for diagnosis of hepatitis C infection and compositions and methods of screening for modulators of hepatitis C infection

IN Tom, Edward Yat Wah; Zlotnik, Albert; Kershenovich, David

PA Eos Biotechnology, Inc., USA

SO PCT Int. Appl., 230 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT	2	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	----	-----	-----

PI WO 2003022987 A2 20030320 WO 2002-XA23914  
20020724 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG WO  
2003022987 A2 20030320 WO 2002-US23914  
20020724 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,



KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US  
2003228570 A1 20031211 US 2003-366435

20030212

PRAI US 2001-308188P P 20010726 US 2002-366782P  
P 20020321 WO 2002-US23914 A 20020724 US  
2002-206473 B1 20020724

AB Described herein are genes whose expression are up-regulated or down-regulated during the course of hepatitis C infection, or distinction between treatment response. Gene expression profiles are selected from 58,680 probesets in the Affymetrix/Eos Hu03 GeneChip array using samples of hepatitis C-pos. and hepatitis C-neg. liver. Markers are also identified which correlate with subsets of patients who respond to treatment with interferon-.alpha./ribavirin, or with subsets of patients who are retractile (non-responsive) to treatment with std. interferon-.alpha. treatment. Related methods and compns. that can be used for diagnosis and treatment of hepatitis C infection and/or its secondary consequences are disclosed. Also described herein are methods that can be used to identify modulators of hepatitis C infection and/or its secondary consequences. [This abstr. record is one of two records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 85 OF 169 CAPLUS COPYRIGHT 2005 ACS ON STN  
AN 2003:271184 CAPLUS  
DN 139:307251

TI Global \*\*\*expression\*\*\* \*\*\*profiling\*\*\* of sulfur-starved Arabidopsis by DNA microarray reveals the role of O-acetyl-L-serine as a general regulator of gene expression in response to sulfur nutrition

AU Hirai, Masami Yokota; Fujiwara, Toru; Awazuhara, Motoko; Kimura, Tomoko; Noji, Masaaki; Saito, Kazuki

CS Department of Molecular Biology and Biotechnology, Graduate School of Pharmaceutical Sciences, Chiba University, Inage-ku, Chiba, 263-8522, Japan

SO Plant Journal (2003), 33(4), 651-663 CODEN: PLJUED; ISSN: 0960-7412

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB To investigate the changes in profiles of mRNA accumulation in response to sulfur deficiency, approx. 13,000 nonredundant Arabidopsis thaliana ESTs corresponding to approx. 9000 genes were analyzed using DNA microarray. Three-week-old Arabidopsis plants grown on an agarose-solidified control medium were transferred to a sulfate-free medium and grown for 48 h for the analyses of sulfur-related metabolites and global \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. Concns. of sulfate, O-acetyl-L-serine (OAS), a pos. regulator of sulfur deficiency-responsive genes, cysteine, and glutathione (GSH) were detd. Plants transferred to sulfate-free media had reduced concns. of sulfate and GSH, and OAS concns. increased. Macroarray anal. revealed a no. of genes, including APR2 and Sultr1;2, whose mRNA accumulation was increased by sulfur deficiency. Profiling was also carried out with plants treated with OAS under sulfate-sufficient condition. Scatter plot anal. revealed a pos. \*\*\*correlation\*\*\* between the changes of expression levels by sulfur deficiency and by OAS treatment

among the clones \*\*\*tested\*\*\*, suggesting that mRNA accumulation of a no. of genes under sulfur deficiency is mainly controlled by OAS concns. in tissues. It was also revealed that the sets of genes regulated under sulfur deficiency in leaves and roots differ considerably.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 86 OF 169 CAPLUS COPYRIGHT 2005 ACS ON STN  
AN 2003:265542 CAPLUS  
DN 139:301448

TI Effect of retinoic acid on cell proliferation-related gene expression in Raji cells induced by 12-O-tetra-decanoylphorbol-13-acetate

AU Ichiishi, Eiichi; Yoshikawa, Toshikazu; Takai, Takako; Tokuda, Harukuni; Yoshida, Yasuhiko; Hanashiro, Kaoru;

Kaminuma, Tsuguchika; Yoshida, Norimasa; Nishino, Hoyoku  
CS First Department of Medicine, Kyoto Prefectural University of Medicine, Kyoto, 602-8566, Japan

SO Journal of Clinical Biochemistry and Nutrition (2001), 30, 21-31 CODEN: JCBNER; ISSN: 0912-0009

PB Institute of Applied Biochemistry

DT Journal

LA English

AB The Epstein-Barr (EB) virus early antigen expression inhibition \*\*\*test\*\*\* on Raji cells is accepted worldwide as a useful \*\*\*assay\*\*\* system for screening of cancer chemopreventive agents, and the results obtained with it \*\*\*correlate\*\*\* somewhat with those of in vivo screening by the mouse skin \*\*\*test\*\*\*. In this study, to investigate the mechanism of cancer chemoprevention by retinoic acid, we demonstrated the effect of retinoic acid on gene expression induced in Raji cells by 12-O-tetra-decanoylphorbol-13-acetate by using DNA chip technol. We found significant changes in the levels of 322 mRNAs in the cells. Down-regulated genes numbered 109, and up-regulated ones 213. In addn., we evaluated a large no. of genes expressed in Raji cells in response to retinoic acid by using a Cell Signaling Network Database (CSNDB) and thereby extd. 21 interesting genes. The retinoic acid responsiveness of these 21 genes in Raji cells is a new finding. We also found three candidates of signaling pathways through examg. the enormous gene expression data. This trial may be invaluable for DNA chip/microarray users because of our new methodol. using combined array data and database information.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 87 OF 169 CAPLUS COPYRIGHT 2005 ACS ON STN  
AN 2003:242437 CAPLUS  
DN 138:249938

TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* biomarkers and therapeutic targets for brain aging and age-related cognitive impairment in rats

IN Landfield, Philip W.; Blalock, Eric M.; Chen, Kuey-Chu; Foster, Thomas C.

PA University of Kentucky Research Foundation, USA

SO PCT Int. Appl., 84 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	---	-----	-----
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PI WO 2003025122 A2 20030327 WO 2002-US25607  
20020813 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,  
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,  
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,  
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ,  
SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,  
GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI,  
CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
PRAI US 2001-311343P P 20010813

AB A statistical and functional \*\*\*correlation\*\*\* strategy is provided to identify changes in cellular pathways specifically linked to impaired cognitive function with aging. Analyses using the strategy identified multiple groups of genes expressed in the hippocampal CA1 region of rats, where the genes were expressed at different levels for several ages. The aging changes in expression began before mid-life. Many of the genes were involved in specific neuronal and glial pathways with previously unrecognized relationships to aging and/or cognitive decline. The processes identified by the strategy suggest a new hypothesis of brain aging in which initially decreased neuronal activity and/or oxidative metab. trigger sep. but parallel genomic cascades in neurons and glia. In neurons, the cascade results in elevations in calcium signaling and redns. of immediate early gene signaling, biosynthesis, synaptogenesis, and neurite remodeling. In contrast, glia undergo increased lipid metab. and mediate a cycle of demyelination and remyelination that induces antigen presentation, inflammation, oxidative stress, and extracellular restructuring. These identified genes and the proteins they encode can be used as novel biomarkers of brain aging and as targets for developing treatment methods against age-related cognitive decline, Alzheimer's disease, and Parkinson's disease.

L9 ANSWER 88 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:238958 CAPLUS  
DN 139:34182

TI \*\*\*Expression\*\*\* \*\*\*profile\*\*\* of genes from 12p in  
\*\*\*testicular\*\*\* germ cell tumors of adolescents and adults  
associated with i(12p) and amplification at 12p11.2-p12.1  
AU Rodriguez, S.; Jafer, O.; Goker, H.; Summersgill, B. M.;  
Zafarana, G.; Gillis, A. J. M.; van Gurp, R. J. H. L. M.; Oosterhuis,  
J. W.; Lu, Y.-J.; Huddart, R.; Cooper, C. S.; Clark, J.; Looijenga, L.  
H. J.; Shipley, J. M.

CS Molecular Cytogenetics, Institute of Cancer Research,  
Surrey, UK  
SO Oncogene (2003), 22(12), 1880-1891 CODEN: ONCNES;  
ISSN: 0950-9232

PB Nature Publishing Group

DT Journal

LA English

AB Gain of 12p material is invariably assocd. with  
\*\*\*testicular\*\*\* germ cell tumors (TGCTs) of adolescents and  
adults, most usually as an isochromosome 12p. We analyzed  
TGCTs with i(12p) using a global approach to \*\*\*expression\*\*\*  
\*\*\*profiling\*\*\* targeting chromosomes (comparative expressed  
sequence hybridization, CESH). This indicated overexpression of  
genes from 12p11.2-p12.1 relative to \*\*\*testis\*\*\* tissue and  
fibroblasts. The nonseminoma subtype showed higher levels of  
expression than seminomas. Notably, 12p11.2-p12.1 is amplified  
in about 10% of TGCTs and CESH anal. of such amplicon cases  
showed high levels of overexpression from this region.  
Microarray anal., including cDNA clones representing most  
UniGene clusters from 12p11.2-p12.1, was applied to DNA and

RNA from 5 TGCTs with amplification of 12p11.2-p12.1 and  
seven TGCTs with gain of the entire short arm of chromosome  
12. \*\*\*Expression\*\*\* \*\*\*profiles\*\*\* were consistent with  
the CESH data and overexpression of EST595078, MRPS35 and  
LDHB at 12p11.2-p12.1 was detected in most TGCTs. High-level  
overexpression of BCAT1 was specific to nonseminomas and  
overexpression of genes such as CMAS, EK11, KRAS2, SURB7 and  
various ESTs \*\*\*correlated\*\*\* with their amplification. Genes  
such as CCND2, GLU3, LRP6 and HPH1 at 12p13 were also  
overexpressed. The overexpressed sequences identified,  
particularly those in the region amplified, represent candidate  
genes for involvement in TGCT development.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 89 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:221800 CAPLUS  
DN 138:249907

TI Gene expression profiles useful for diagnosis of hepatitis C  
infection and compositions and methods of screening for  
modulators of hepatitis C infection

IN Tom, Edward Yat Wah; Zlotnik, Albert; Kershenobich, David  
PA Eos Biotechnology, Inc., USA

SO PCT Int. Appl., 230 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	-----	-----

PI WO 2003022987 A2 20030320 WO 2002-US23914  
20020724 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,  
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,  
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,  
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM,  
ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,  
GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI,  
CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG WO  
2003022987 A2 20030320 WO 2002-XA23914

20020724 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,  
BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,  
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,  
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,  
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM,  
ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,  
GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI,  
CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US  
2003228570 A1 20031211 US 2003-366435

20030212  
PRAI US 2001-308188P P 20010726 US 2002-366782P  
P 20020321 US 2002-206473 B1 20020724 WO  
2002-US23914 A 20020724

AB Described herein are genes whose expression are up-  
regulated or down-regulated during the course of hepatitis C  
infection, or distinction between treatment response. Gene  
expression profiles are selected from 58,680 probesets in the  
Affymetrix/Eos Hu03 GeneChip array using samples of hepatitis  
C-pos. and hepatitis C-neg. liver. Markers are also identified  
which correlate with subsets of patients who respond to

treatment with interferon- $\alpha$ /ribavirin, or with subsets of patients who are retractile (non-responsive) to treatment with std. interferon- $\alpha$ . treatment. Related methods and compns. that can be used for diagnosis and treatment of hepatitis C infection and/or its secondary consequences are disclosed. Also described herein are methods that can be used to identify modulators of hepatitis C infection and/or its secondary consequences. [This abstr. record is one of two records for this document necessitated by the large no. of index entries required to fully index the document and publication system constraints.].

L9 ANSWER 90 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:219082 CAPLUS DN 139:290519

TI Renal mRNA Levels as Prognostic Tools in Kidney Diseases

AU Eikmans, Michael; Baelde, Hans J.; Hagen, E. Chris; Paul, Leendert C.; Eilers, Paul H. C.; de Heer, Emile; Bruijn, Jan A.

CS Department of Pathology and Medical Statistics, Leiden University Medical Center, Leiden, Neth.

SO Journal of the American Society of Nephrology (2003), 14(4), 899-907 CODEN: JASNEU; ISSN: 1046-6673

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Mol. biol. techniques are currently considered as new diagnostic and prognostic parameters with a sensitivity and specificity exceeding those of histol. and functional data currently used in clin. practice. The results in various clin. settings have been of limited value up to now. This study is an investigation of the use of tissue levels of RNA detd. in routine clin. kidney biopsies as prognostic tools. The focus was on RNA encoding for mols. known to be involved in the pathogenesis of renal disorders. Fresh kidney biopsy tissue was obtained from 52 patients with various renal diseases. The GFR was followed for 12 mo. The extent of glomerulosclerosis and interstitial fibrosis in the biopsies was detd. with quant. digital image anal. Glomerular and tubulointerstitial compartments from each biopsy specimen were sepd., and mRNA levels of TGF- $\beta$ , collagen I, collagen IV, and fibronectin were quantitated by real-time PCR.

\*\*\*Correlations\*\*\*, along with 95% confidence intervals (CI), between all variables \*\*\*tested\*\*\* at time biopsy were detd. To assess their prognostic value, these variables were \*\*\*correlated\*\*\* with the slope of GFR within several time intervals after biopsy. In addn., to evaluate the predictive value of the variables for outcome in individual patients, differences for each variable were \*\*\*tested\*\*\* between patients showing progressive decline in renal function (slope GFR < 0) and patients showing stable or improving renal function over time (slope GFR .gtoreq. 0). In chronic renal diseases, the extent of histol. damage \*\*\*correlated\*\*\* with the GFR at the time of biopsy ( $r = -0.44$ ; CI  $-0.68$  to  $-0.11$ ), but it did not \*\*\*correlate\*\*\* with the slope expressing a change in GFR after the biopsy. Tubulointerstitial TGF- $\beta$ . mRNA levels \*\*\*correlated\*\*\* with the rate of change in GFR between time of biopsy and 1 mo later ( $r = 0.41$ ; CI,  $0.07$  to  $0.67$ ). The GFR at the time of biopsy \*\*\*correlated\*\*\* with the slope of change in GFR between time of biopsy and 12 mo later ( $r = -0.50$ ; CI,  $-0.73$  to  $-0.18$ ). In chronic renal diseases, glomerular fibronectin mRNA levels, in comparison with the GFR at time of biopsy, \*\*\*correlated\*\*\* relatively strongly with the slope of change in GFR between 3 and 12 mo ( $r = 0.50$ ; CI,  $0.16$  to  $0.74$ ). Patients with favorable renal outcome after 12 mo showed significantly higher TGF- $\beta$ . mRNA levels and lower proteinuria levels at time of biopsy ( $P < 0.05$ ) than patients with a progressive decline in renal function. This study shows that mRNA levels measured in kidney biopsies can function as prognostic tools in human renal diseases. In

particular, relatively high levels of tubulointerstitial TGF- $\beta$ . mRNA and glomerular fibronectin mRNA are assocd. with less deterioration in renal function.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 91 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:198707 CAPLUS

DN 139:48523

TI Decreased DNA repair gene expression among individuals exposed to arsenic in United States drinking water

AU Andrew, Angeline S.; Karagas, Margaret R.; Hamilton, Joshua W.

CS Department of Community and Family Medicine, Dartmouth Medical School, Lebanon, NH, 03756, USA

SO International Journal of Cancer (2003), 104(3), 263-268

CODEN: IJCNW; ISSN: 0020-7136

PB Wiley-Liss, Inc.

DT Journal

LA English

AB Arsenic is well established as a human carcinogen, but its precise mechanism of action remains unknown. Arsenic does not directly damage DNA, but may act as a carcinogen through inhibition of DNA repair mechanisms, leading indirectly to increased mutations from other DNA damaging agents. The mol. mechanism underlying arsenic inhibition of nucleotide excision repair after UV irradiation (A. Hartwig et al., 1997) is unknown, but could be due to decreased expression of crit. genes involved in nucleotide excision repair of damaged DNA. This hypothesis was \*\*\*tested\*\*\* by analyzing expression of repair genes and arsenic exposure in a subset of 16 individuals enrolled in a population based case-control study investigating arsenic exposure and cancer risk in New Hampshire. Toenail arsenic levels were inversely \*\*\*correlated\*\*\* with expression of crit. members of the nucleotide excision repair complex, ERCCI ( $r_2 = 0.82$ ,  $p < 0.0001$ ), XPF ( $r_2 = 0.56$ ,  $p < 0.002$ ), and XPB ( $r_2 = 0.75$ ,  $p < 0.0001$ ). The internal dose marker, toenail arsenic level, was more strongly assocd. with changes in expression of these genes than drinking water arsenic concn. Our findings, based on human exposure to arsenic in a US population, show an assocn. between biomarkers of arsenic exposure and expression of DNA repair genes. Although our findings need verification in a larger study group, they are consistent with the hypothesis that inhibition of DNA repair capacity is a potential mechanism for the co-carcinogenic activity of arsenic.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 92 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:190275 CAPLUS

DN 138:399515

TI Patterns of expression of chromosome 17 genes in primary cultures of normal ovarian surface epithelia and epithelial ovarian cancer cell lines

AU Presneau, Nadege; Mes-Masson, Anne-Marie; Ge, Bing; Provencher, Diane; Hudson, Thomas J.; Tonin, Patricia N.

CS Research Institute of the McGill University Health Centre, Montreal, QC, H3G 1A4, Can.

SO Oncogene (2003), 22(10), 1568-1579 CODEN: ONCNES; ISSN: 0950-9232

PB Nature Publishing Group

DT Journal

LA English

AB Oligonucleotide microarray anal. was applied to assess the \*\*\*expression\*\*\* \*\*\*profile\*\*\* of 332 probe sets representing 308 genes or expressed sequence tags (ESTs) that map to chromosome 17 to address epigenetic events that result in alterations in gene expression in epithelial ovarian cancer (EOC). \*\*\*Expression\*\*\* \*\*\*profiles\*\*\* were generated from 12 primary cultures derived from normal ovarian surface epithelium (NOSE) and four long-term cultures (TOV-81D, TOV-112D, TOV-21G and OV-90) derived from EOCs that have been previously characterized and shown to mimic features of the tumoral cells from which they were derived. The expression values of all 332 probe sets is highly \*\*\*correlated\*\*\* across the 12 NOSEs (89% \*\*\*correlation\*\*\* coeffs. >0.90). In two-way comparisons, differential \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* were obsd. for 157 probe sets for which the expression value of at least one EOC cell line fell outside the limits of the range of expression of the 12 NOSEs. When compared to NOSEs, four genes displayed similar differential \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* across all four EOC cell lines, and 26 genes displayed similar differential \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* across the three EOC cell lines (TOV-112D, TOV-21G and OV-90) representing tumoral cells derived from the most aggressive disease. A total of 17 genes displayed differential \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* greater than threefold in at least one EOC cell line in comparison to NOSE, and three genes were differentially expressed greater than threefold across all aggressive cell lines. The anal. of a selected no. of genes by RT-PCR revealed \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* comparable to those obsd. by microarray anal. in the majority of samples \*\*\*tested\*\*\*. Comparison of \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of differentially expressed genes identified by microarray anal. in two-way comparisons of the EOC cell lines and the NOSEs with published reports revealed 10 genes previously implicated in ovarian tumorigenesis and 18 in tumorigenesis of other types of cancer. The differential \*\*\*pattern\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* of genes that map to both the p and q arm of chromosome 17 is consistent with the hypothesis that a no. of genes that map to this chromosome are implicated in the etiol. of ovarian cancer.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 93 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:179401 CAPLUS

TI Design of experiments based on pharmacogenomics analysis of databases containing \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* and compound activities to help elucidate molecular mechanisms

AU Yang, Chihai; Blower, Paul; Brueggemeier, Robert W.; Richards, Jeanette A.

CS LeadScope, Inc., Columbus, OH, 43212, USA

SO Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), BTEC-019 Publisher: American Chemical Society, Washington, D. C. CODEN: 69DSA4

DT Conference; Meeting Abstract

LA English

AB High throughput genomic studies are producing large databases of mol. information on cancers and other cell and tissue types. Hence, the opportunity to link these accumulating data to the drug discovery process becomes a real possibility. However, despite the introduction of a new paradigm and methodologies, this large amt. of information and significant

investment has not led to dramatic increases in productivity in drug discovery. In the past, we have \*\*\*correlated\*\*\* the \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of NCI 60 cell lines to compd. activity patterns of the same cell lines. Genes in specific biol. process pathways were \*\*\*correlated\*\*\* with certain chem. scaffolds, whose assocns. were used to build mol. hypotheses. The gene selection was carried out using a gene hierarchy built on annotations from the Gene Ontol. Consortium; the hierarchical classification based on biol. process was used to differentiate \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\* of various cell types. The chem. scaffolds are built by extg. common cores of the compds. responsible for the initial \*\*\*correlations\*\*\* with \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. These compd. scaffolds are used to probe the genes within certain pathways. The set of selected genes and the compds. provide a foundation for building hypotheses based on mol. mechanisms. Concg. on the data mining results from breast cancer cell lines, design of further expts. to actually \*\*\*test\*\*\* the mol. hypothesis of pairs of compd. and genes will be discussed.

L9 ANSWER 94 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:166747 CAPLUS  
DN 138:396955

TI Comparative gene analysis of *Biomphalaria glabrata* hemocytes pre- and post-exposure to miracidia of *Schistosoma mansoni*

AU Raghavan, Nithya; Miller, Andre N.; Gardner, Malcolm; FitzGerald, Peter C.; Kerlavage, Anthony R.; Johnston, David A.; Lewis, Fred A.; Knight, Matty

CS Biomedical Research Institute, Rockville, MD, 20852, USA

SO Molecular and Biochemical Parasitology (2003), 126(2), 181-191 CODEN: MBIPDP; ISSN: 0166-6851

PB Elsevier Science B.V.

DT Journal

LA English

AB The internal defense mechanism of the snail *Biomphalaria glabrata* during a schistosome infection is activated and mediated via the immune effector cells known as hemocytes. Since resistance and susceptibility to schistosome infection is known to be genetically detd., our interest was to use the EST approach as a gene discovery tool to examine transcription profiles in hemocytes of resistant snails pre- and post-exposure to *Schistosoma mansoni*. Comparative anal. of the transcripts suggested that parasite exposure caused an active metabolic response in the hemocytes. The most abundant transcripts were those showing 23-74% similarity to known reverse transcriptases (RT). Further characterization by RT-PCR indicated the RT transcripts were expressed in normal snails, parasite exposed snails, and the embryonic cell line Bge. To det. whether the occurrence of RT transcripts \*\*\*correlates\*\*\* to the presence of functional enzyme activity in the snails, RT \*\*\*assays\*\*\* were performed from both resistant and susceptible snails, pre- and post-exposure to miracidia, using protein exts. from the head-foot and posterior region tissues. Results indicated that in the resistant snail, RT activity was greater in the posterior region than in the head-foot. After exposure, however, RT activity increased dramatically in the head-foot, with peak activity at 24 h post-exposure. The detection of RT activity in *B. glabrata* was unexpected and the role of this enzyme in the hemocyte-mediated killing of parasites is not yet known. However, identification of this and other transcripts from these cells by the EST approach provides a useful resource towards elucidating the mol. basis of resistance/susceptibility in this snail-host parasite relationship.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 95 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:164376 CAPLUS  
DN 138:352511

TI Temporal changes in cytokine expression of foals during the  
first month of life

AU Boyd, N. K.; Cohen, N. D.; Lim, W.-S.; Martens, R. J.;  
Chaffin, M. K.; Ball, J. M.

CS College of Veterinary Medicine, Department of Veterinary  
Pathobiology, Texas A&M University, College Station, TX, 77843-  
4467, USA

SO Veterinary Immunology and Immunopathology (2003),  
92(1-2), 75-85 CODEN: VIIMDS; ISSN: 0165-2427

PB Elsevier Science B.V.

DT Journal

LA English

AB Foals are uniquely susceptible to a wide variety of  
opportunistic infections normally assocd. with  
immunodeficiencies. Little is understood about the immune  
system of foals during the neonatal period. An apparent age-  
related susceptibility predisposes neonatal foals to infectious  
diseases and hinders therapeutic and preventative interventions  
for these diseases. Cytokine expression is \*\*\*correlated\*\*\*  
with the type of immune response as well as the severity of a  
disease. In this study, we measured foal peripheral blood  
mononuclear cell (PBMC)-specific mRNA cytokine expression from  
72 foals from three different farms during the first 4 wk of life.  
Interleukin-1.alpha. (IL-1.alpha.), IL-1.beta., IL-2, IL-4, IL-6, IL-  
8, IL-10, IL-12p35, IL-12p40, interferon-.gamma. (IFN-.gamma.),  
tumor necrosis factor-.alpha. (TNF-.alpha.), and transforming  
growth factor-.beta.1 (TGF-.beta.1) were cloned and transcribed  
in vitro to generate antisense probes for RNase protection  
\*\*\*assays\*\*\*. Using linear mixed-effect models, we detd. that  
IFN-.gamma., TGF-.beta.1, and IL-1.alpha. increased significantly  
(P<0.05) with age.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 96 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:163998 CAPLUS  
DN 138:332418

TI Assessing unmodified 70-mer oligonucleotide probe  
performance on glass-slide microarrays

AU Wang, Hong-Ying; Malek, Renae L.; Kwitek, Anne E.;  
Greene, Andrew S.; Luu, Truong V.; Behbahani, Babak; Frank,  
Bryan; Quackenbush, John; Lee, Norman H.

CS The Institute for Genomic Research, Rockville, MD, 20850,  
USA

SO GenomeBiology (2002), 4(1), No pp. given CODEN:  
GNBLFW; ISSN: 1465-6914 URL:

<http://genomebiology.com/content/pdf/gb-2003-4-1-r5.pdf>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Long oligonucleotide microarrays are potentially more cost-  
and management-efficient than cDNA microarrays, but there is  
little information on the relative performance of these two probe  
types. The feasibility of using unmodified oligonucleotides to  
accurately measure changes in gene expression is also unclear.  
Unmodified sense and antisense 70-mer oligonucleotides  
representing 75 known rat genes and 10 Arabidopsis control  
genes were synthesized, printed and UV cross-linked onto glass

slides. Printed alongside were PCR-amplified cDNA clones  
corresponding to the same genes, enabling us to compare the  
two probe types simultaneously. Our study was designed to  
evaluate the mRNA profiles of heart and brain, along with  
Arabidopsis cRNA spiked into the labeling reaction at different  
relative copy no. Hybridization signal intensity did not  
\*\*\*correlate\*\*\* with probe type but depended on the extent of  
UV irradiation. To det. the effect of oligonucleotide concn. on  
hybridization signal, 70-mers were serially dild. No significant  
change in gene-expression ratio or loss in hybridization signal  
was detected, even at the lowest concn. \*\*\*tested\*\*\* (6.25  
.mu.M). In many instances, signal intensity actually increased  
with decreasing concn. The \*\*\*correlation\*\*\* coeff. between  
oligonucleotide and cDNA probes for identifying differentially  
expressed genes was 0.80, with an av. coeff. of variation of  
13.4%. Approx. 8% of the genes showed discordant results with  
the two probe types, and in each case the cDNA results were  
more accurate, as detd. by real-time PCR. Microarrays of UV  
cross-linked unmodified oligonucleotides provided sensitive and  
specific measurements for most of the genes studied.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 97 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2003:150080 CAPLUS

DN 138:319023

TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\* vary  
in clonal cell cultures from Rett syndrome females with eight  
different MECP2 mutations

AU Traynor, Jeff; Agarwal, Priyanka; Lazzeroni, Laura; Francke,  
Uta

CS Department of Genetics, Stanford University School of  
Medicine, Stanford, CA, 94305, USA

SO BMC Medical Genetics [online computer file] (2002), 3, No  
pp. given CODEN: BMGMAR; ISSN: 1471-2350 URL:

<http://www.biomedcentral.com/1471-2350/3/12>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Background: Females with the neurol. disorder Rett  
syndrome are heterozygous for mutations in X-linked MECP2 that  
encodes methyl-CpG binding protein 2 (MeCP2) thought to act as  
a transcriptional repressor. To identify target genes for MeCP2  
modulation, the authors studied global gene expression in single  
cell-derived wild-type and mutant MECP2 expressing fibroblast  
clones with four common mutations (R106W, R306C, 705delG,  
1155del32) and in lymphoblastoid cell lines (LCLs) that included  
four mutant MeCP2 (T158M, 803delG, R168X and 1159del28)  
expressing, and five (1159del28, R106W, R255X, 803delG,  
803delG) wild-type MeCP2 expressing lines. Methods: Clonality  
and mutation status were verified by androgen receptor  
methylation \*\*\*assays\*\*\* for X-inactivation and by  
sequencing MECP2 transcripts. Expression studies were done  
with oligonucleotide microarrays (Affymetrix U95) and verified  
with real-time quant. RT-PCR using Sybr Green. Results:  
Expression of 49 transcripts was increased, and expression of 21  
transcripts was decreased, in at least 3 of 4 mutant/wild-type  
fibroblast comparisons. Transcript levels of 11 genes, detd.  
quant. RT-PCR, were highly \*\*\*correlated\*\*\* with the  
microarray data. Therefore, multiple addnl. clones from two Rett  
individuals were \*\*\*tested\*\*\* by RT-PCR only. Striking  
expression differences were found in both mutant and wildtype  
MeCP2 expressing clones. Comparing \*\*\*expression\*\*\*  
\*\*\*profiles\*\*\* of lymphoblastoid cell lines yielded 16  
differentially expressed genes. Conclusions: MeCP2 deficiency

does not lead to global deregulation of gene expression. Either MeCP2's in vivo function does not involve widespread transcriptional repression, or its function is redundant in cell types that also express other methyl-CpG binding proteins. The data suggest that clonal fibroblast strains may show substantial inter-strain variation, making them a difficult and unstable resource for genome-wide \*\*\*expression\*\*\* \*\*\*profiling\*\*\* studies.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 98 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:146172 CAPLUS DN 138:381837

TI Carbohydrate-induced Differential \*\*\*Gene\*\*\* \*\*\*Expression\*\*\* \*\*\*Patterns\*\*\* in the Hyperthermophilic Bacterium *Thermotoga maritima*

AU Chhabra, Swapnil R.; Shockley, Keith R.; Connors, Shannon B.; Scott, Kevin L.; Wolfinger, Russell D.; Kelly, Robert M.

CS Department of Chemical Engineering, North Carolina State University, Raleigh, NC, 27695, USA

SO Journal of Biological Chemistry (2003), 278(9), 7540-7552 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB The hyperthermophilic bacterium *Thermotoga maritima* MSB8 was grown on a variety of carbohydrates to det. the influence of carbon and energy source on differential gene expression. Despite the fact that *T. maritima* has been phylogenetically characterized as a primitive microorganism from an evolutionary perspective, results here suggest that it has versatile and discriminating mechanisms for regulating and effecting complex carbohydrate utilization. Growth of *T. maritima* on monosaccharides was found to be slower than growth on polysaccharides, although growth to cell densities of 108 to 109 cells/mL was obsd. on all carbohydrates

\*\*\*tested\*\*\* Differential expression of genes encoding carbohydrate-active proteins encoded in the *T. maritima* genome was followed using a targeted cDNA microarray in conjunction with mixed model statistical anal. Coordinated regulation of genes responding to specific carbohydrates was noted. Although glucose generally repressed expression of all glycoside hydrolase genes, other sugars induced or repressed these genes to varying extents. \*\*\*Expression\*\*\* \*\*\*profiles\*\*\* of most endo-acting glycoside hydrolase genes \*\*\*correlated\*\*\* well with their reported biochem. properties, although exo-acting glycoside hydrolase genes displayed less specific expression patterns. Genes encoding selected putative ABC sugar transporters were found to respond to specific carbohydrates, and in some cases putative oligopeptide transporter genes were also found to respond to specific sugar substrates. Several genes encoding putative transcriptional regulators were expressed during growth on specific sugars, thus suggesting functional assignments. The transcriptional response of *T. maritima* to specific carbohydrate growth substrates indicated that sugar backbone- and linkage-specific regulatory networks are operational in this organism during the uptake and utilization of carbohydrate substrates. Furthermore, the wide ranging collection of such networks in *T. maritima* suggests that this organism is capable of adapting to a variety of growth environments contg. carbohydrate growth substrates.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 99 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:119697 CAPLUS DN 138:301667

TI Molecular determinants of tumor differentiation in papillary serous ovarian carcinoma

AU Jazaeri, Amir A.; Lu, Karen; Schmandt, Rosemarie; Harris, Charles P.; Rao, Pulivarthi H.; Sotiriou, Christos; Chandramouli, G. V. R.; Gershenson, David M.; Liu, Edison T.

CS Center for Cancer Research of the National Cancer Institute, Gaithersburg, MD, USA

SO Molecular Carcinogenesis (2003), 36(2), 53-59 CODEN: MOCAE8; ISSN: 0899-1987

PB Wiley-Liss, Inc.

DT Journal

LA English

AB In epithelial ovarian cancer, tumor grade is an independent prognosticator whose mol. determinants remain unknown. The authors investigated \*\*\*patterns\*\*\* of \*\*\*gene\*\*\* \*\*\*expression\*\*\* in well- and poorly differentiated serous papillary ovarian and peritoneal carcinomas with cDNA microarrays. A 6500-feature cDNA microarray was used for comparison of the mol. profiles of eight grade III and four grade I stage III serous papillary adenocarcinomas. With a modified F-\*\*\*test\*\*\* in conjunction with random permutations, 99 genes whose expression was significantly different between grade I and grade III tumors were identified. A disproportionate no. of these differentially expressed genes were located on the chromosomal regions 20q13 and all exhibited higher expression in grade III tumors. Interphase fluorescent in situ hybridization demonstrated 20q13 amplification in two of the four grade III and none of the three grade I tumors available for evaluation. Several centrosome-related genes also showed higher expression in grade III tumors. The authors propose a model in which tumor differentiation is inversely \*\*\*correlated\*\*\* with the overexpression of several oncogenes located on 20q13, a common amplicon in ovarian and numerous other cancers. Dysregulation of centrosome function is one potential mechanistic link between genetic/epigenetic changes and the poorly differentiated phenotype in ovarian cancer.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 100 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN AN 2003:119333 CAPLUS

DN 139:33667

TI Molecular features of adult mouse small intestinal epithelial progenitors

AU Stappenbeck, Thaddeus S.; Mills, Jason C.; Gordon, Jeffrey I.

CS Department of Molecular Biology and Pharmacology, Washington University School of Medicine, St. Louis, MO, 63110, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(3), 1004-1009 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB The adult mouse small intestinal epithelium undergoes perpetual regeneration, fueled by a population of multipotential stem cells and oligopotential daughters located at the base of crypts of Lieberkuhn. Although the morphol. features of small intestinal epithelial progenitors (SIEPs) are known, their mol.



features are poorly defined. Previous impediments to purifn. and mol. characterization of SiEPs include lack of ex vivo clonogenic \*\*\*assays\*\*\* and the difficulty of phys. retrieving them from their niche where they are interspersed between their numerous differentiated Paneth cell daughters. To overcome these obstacles, we used germ-free transgenic mice lacking Paneth cells to obtain a consolidated population of SiEPs with normal proliferative activity. These cells were harvested by laser capture microdissection. Functional genomics anal. identified 163 transcripts enriched in SiEPs compared with Paneth cell-dominated normal crypt base epithelium. The dataset was validated by (i) \*\*\*correlation\*\*\* with the organellar compn. of SiEPs vs. Paneth cells, (ii) similarities to databases generated from recent mouse hematopoietic and neural stem cell genome anatomy projects, and (iii) laser capture microdissection/real-time quant. RT-PCR studies of progenitor cell-contg. populations retrieved from the small intestines, colons, and stomachs of conventionally raised mice. The SiEP profile has prominent representation of genes involved in c-myc signaling and in the processing, localization, and translation of mRNAs. This dataset, together with our recent anal. of gene expression in the gastric stem cell niche, discloses a set of mol. features shared by adult mouse gut epithelial progenitors.

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 101 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:119104 CAPLUS

DN 138:350908

TI Molecular analysis of a *Saccharomyces cerevisiae* mutant with improved ability to utilize xylose shows enhanced expression of proteins involved in transport, initial xylose metabolism, and the pentose phosphate pathway

AU Wahlbom, C. Fredrik; Otero, Ricardo R. Cordero; van Zyl, Willem H.; Hahn-Hagerdal, Barbel; Jonsson, Leif J.

CS Department of Applied Microbiology, Lund University, Lund, 221 00, Swed.

SO Applied and Environmental Microbiology (2003), 69(2), 740-746 CODEN: AEMIDF; ISSN: 0099-2240

PB American Society for Microbiology

DT Journal

LA English

AB Differences between the recombinant xylose-utilizing *Saccharomyces cerevisiae* strain TMB 3399 and the mutant strain TMB 3400, derived from TMB 3399 and displaying improved ability to utilize xylose, were investigated by using genome-wide expression anal., physiol. characterization, and biochem. \*\*\*assays\*\*\*. Samples for anal. were withdrawn from chemostat cultures. The characteristics of *S. cerevisiae* TMB 3399 and TMB 3400 grown on glucose and on a mixt. of glucose and xylose, as well as of *S. cerevisiae* TMB 3400 grown on only xylose, were investigated. The strains were cultivated under chemostat conditions at a diln. rate of 0.1 h<sup>-1</sup>, with feeds consisting of a defined mineral medium supplemented with 10 g of glucose liter<sup>-1</sup>, 10 g of glucose plus 10 g of xylose liter<sup>-1</sup> or, for *S. cerevisiae* TMB 3400, 20 g of xylose liter<sup>-1</sup>. *S. cerevisiae* TMB 3400 consumed 31% more xylose of a feed contg. both glucose and xylose than *S. cerevisiae* TMB 3399. The biomass yields for *S. cerevisiae* TMB 3400 were 0.46 g of biomass g of consumed carbohydrate-1 on glucose and 0.43 g of biomass g of consumed carbohydrate-1 on xylose. A K<sub>s</sub> value of 33 mM for xylose was obtained for *S. cerevisiae* TMB 3400. In general, the percentage error was <20% between duplicate microarray expts. originating from independent fermn. expts. Microarray anal.

showed higher expression in *S. cerevisiae* TMB 3400 than in *S. cerevisiae* TMB 3399 for (i) HXT5, encoding a hexose transporter; (ii) XKS1, encoding xylulokinase, an enzyme involved in one of the initial steps of xylose utilization; and (iii) SOL3, GND1, TAL1, and TKL1, encoding enzymes in the pentose phosphate pathway. In addn., the transcriptional regulators encoded by YCR020C, YBR083W, and YPR199C were expressed differently in the two strains. Xylose utilization was, however, not affected in strains in which YCR020C was overexpressed or deleted. The higher expression of XKS1 in *S. cerevisiae* TMB 3400 than in TMB 3399 \*\*\*correlated\*\*\* with higher specific xylulokinase activity in the cell exts. The specific activity of xylose reductase and xylitol dehydrogenase was also higher for *S. cerevisiae* TMB 3400 than for TMB 3399, both on glucose and on the mixt. of glucose and xylose.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 102 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:100540 CAPLUS

DN 139:206994

TI Chemogenomics for predictive drug assessment

AU Furness, Mike; Pearson, Cecelia; Natsoulis, George;

Engelberg, Alan; Bostian, Keith; Jarnagin, Kurt

CS Iconix Pharmaceuticals, Mountain View, CA, 94043, USA

SO Toxicogenomics (2003), 204-212. Editor(s): Inoue, Tohru;

Pennie, William D. Publisher: Springer-Verlag Tokyo, Tokyo,

Japan. CODEN: 69DOR9; ISBN: 4-431-70344-6

DT Conference

LA English

AB Improved lead prioritization in relation to toxicity, efficacy and mechanism of action could improve the overall success of drug discovery. DrugMatrix is an integrated database incorporating compd. data including mol. pharmacol., gene expression, chem. structure and SAR, toxicol., pathol., and pharmacol. This database helps drug prioritization by providing the front line of drug discovery (toxicologists, pharmacologists and medicinal chemists) early data about adverse events and potential benefits. We have used DrugMatrix mol. pharmacol. \*\*\*assays\*\*\* and expression findings to classify several nuclear hormone receptor agonists (clofibrate, fenofibrate, gemfibrozil, DEHP, bisphenol-A, estradiol and octylphenol) into groups that mirror their receptor interactions. The gene expression changes that drive these groupings include the fatty acid oxidn. genes. DrugMatrix can further distinguish unique qualities of a single drug within a particular class. Gemfibrozil is contraindicated in hypertriglyceridemic patients due to an unusual elevation of LDL levels. Our studies show that it uniquely elevates fatty acid and cholesterol biosynthesis gene expression. These observations provide a mol. distinction that \*\*\*correlates\*\*\* with the clin. distinction of gemfibrozil from the other compds. and suggest a mechanism behind this distinction. These findings illustrate the value of an early, detailed understanding about adverse events and unappreciated benefits, speeding lead prioritization and selection.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 103 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:93480 CAPLUS

DN 138:332748

TI Evidence for large domains of similarly expressed genes in the *Drosophila* genome

AU Spellman, Paul T.; Rubin, Gerald M.

CS Howard Hughes Medical Institute and Department of Molecular and Cell Biology, University of California, Berkeley, CA, 94720-3400, USA

SO *Journal of Biology* (London, United Kingdom) (2002), 1(1), No pp. given CODEN: JBOIAW; ISSN: 1475-4924 URL: <http://jbiol.com/content/1/1/5>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Transcriptional regulation in eukaryotes generally operates at the level of individual genes. Regulation of sets of adjacent genes by mechanisms operating at the level of chromosomal domains has been demonstrated in a no. of cases, but the fraction of genes in the genome subject to regulation at this level is unknown. *Drosophila* \*\*\*gene\*\*\* - \*\*\*expression\*\*\* \*\*\*profiles\*\*\* that were detd. from over 80 exptl. conditions using high-d. oligonucleotide microarrays were searched for groups of adjacent genes that show similar \*\*\*expression\*\*\* \*\*\*profiles\*\*\*. We found about 200 groups of adjacent and similarly expressed genes, each having between 10 and 30 members; together these groups account for over 20% of \*\*\*assayed\*\*\* genes. Each group covers between 20 and 200 kilobase pairs of genomic sequence, with a mean group size of about 100 kilobase pairs. Groups do not appear to show any \*\*\*correlation\*\*\* with polytene banding patterns or other known chromosomal structures, nor were genes within groups functionally related to one another. Groups of adjacent and co-regulated genes that are not otherwise functionally related in any obvious way can be identified by \*\*\*expression\*\*\* \*\*\*profiling\*\*\* in *Drosophila*. The mechanism underlying this phenomenon is not yet known.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 104 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:90887 CAPLUS

DN 138:281831

TI How many genes are needed for a discriminant microarray data analysis

AU Li, Wentian; Yang, Yaning

CS Laboratory of Statistical Genetics, The Rockefeller University, New York, NY, 10021, USA

SO *Methods of Microarray Data Analysis, Papers from CAMDA '00*, Durham, NC, United States, Dec. 18-19, 2000 (2002), Meeting Date 2000, 137-149. Editor(s): Lin, Simon M.; Johnson, Kimberly F. Publisher: Kluwer Academic Publishers, Norwell, Mass. CODEN: 69DOO6; ISBN: 0-7923-7564-5

DT Conference

LA English

AB The anal. of the leukemia data from Whitehead/MIT group is a discriminant anal. (also called a supervised learning). Among thousands of genes whose expression levels are measured, not all are needed for discriminant anal. A gene may either not contribute to the sepn. of two types of tissues/cancers, or it may be redundant because it is highly \*\*\*correlated\*\*\* with other genes. There are two theor. frameworks in which variable selection (or gene selection in our case) can be addressed. The first is model selection, and the second is model averaging. We have carried out model selection using Akaike information criterion and Bayesian information criterion with logistic regression (discrimination, prediction, or classification) to det. the

no. of genes that provide the best model. These model selection criteria set upper limits of 22.apprx.25 and 12.apprx.13 genes for this data set with 38 samples, and the best model consists of only one (no.4847, zyxin) or two genes. We have also carried out model averaging over the best single-gene logistic predictors using three different wts.: maximized likelihood, prediction rate on training set, and equal wt. We have obsd. that the performance of most of these weighted predictors on the \*\*\*testing\*\*\* set is gradually reduced as more genes are included, but a clear cutoff that separates good and bad prediction performance is not found.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 105 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:47970 CAPLUS

DN 138:282175

TI FlhD/FlhC is a regulator of anaerobic respiration and the Entner-Doudoroff pathway through induction of the methyl-accepting chemotaxis protein Aer

AU Pruss, Birgit M.; Campbell, John W.; Van Dyk, Tina K.; Zhu, Charles; Kogan, Yakov; Matsumura, Philip

CS Department of Microbiology and Immunology, University of Illinois at Chicago, Chicago, IL, 60612-7344, USA

SO *Journal of Bacteriology* (2003), 185(2), 534-543 CODEN: JOBAAY; ISSN: 0021-9193

PB American Society for Microbiology

DT Journal

LA English

AB The regulation by two transcriptional activators of flagellar expression (FlhD and FlhC) and the chemotaxis methyl-accepting protein Aer was studied with glass slide DNA microarrays. An flhD::Kan insertion and an aer deletion were independently introduced into two *Escherichia coli* K-12 strains, and the effects upon gene regulation were investigated. Altogether, the flhD::Kan insertion altered the expression of 29 operons of known function. Among them was Aer, which in turn regulated a subset of these operons, namely, the ones involved in anaerobic respiration and the Entner-Doudoroff pathway. In addn., FlhD/FlhC repressed enzymes involved in aerobic respiration and regulated many other metabolic enzymes and transporters in an Aer-independent manner. Expression of 12 genes of uncharacterized function was also affected. FlhD increased gltBD, gcvTHP, and ompT expression. The regulation of half of these genes was subsequently confirmed with reporter gene fusions, enzyme \*\*\*assays\*\*\*, and real-time PCR. Growth phenotypes of flhD and flhC mutants were detd. with Phenotype MicroArrays and \*\*\*correlated\*\*\* with gene expression.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 106 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:43556 CAPLUS

DN 138:121399

TI T cell chemokine receptor expression in aging

AU Mo, Ruran; Chen, Jun; Han, Yin; Bueno-Cannizares, Cecelia; Misk, David E.; Lescure, Pascal A.; Hanash, Samir; Yung, Raymond L.

CS Divisions of Geriatric Medicine and Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, 48109, USA



SO Journal of Immunology (2003), 170(2), 895-904 CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB Changes in chemokine receptor expression are important in detg. T cell migration and the subsequent immune response. To better understand the contribution of the chemokine system in immune senescence the authors detd. the effect of aging on CD4+ T cell chemokine receptor function using microarray, RNase protection \*\*\*assays\*\*\*, Western blot, and in vitro chemokine transmigration \*\*\*assays\*\*\*. Freshly isolated CD4+ cells from aged (20-22 mo) mice were found to express a higher level of CCR1, 2, 4, 5, 6, and 8 and CXCR2-5, and a lower level of CCR7 and 9 than those from young (3-4 mo) animals. Caloric restriction partially or completely restored the aging effects on CCR1, 7, and 8 and CXCR2, 4, and 5. The aging-assocd. differences in chemokine receptor expression cannot be adequately explained by the age-assocd. shift in the naive/memory or Th1/Th2 profile. CD4+ cells from aged animals have increased chemotactic response to stromal cell-derived factor-1 and macrophage-inflammatory protein-1.alpha., suggesting that the obsd. chemokine receptor changes have important functional consequences. The authors propose that the aging-assocd. changes in T cell chemokine receptor expression may contribute to the different clin. outcome in T cell chemokine receptor-dependent diseases in the elderly.  
RE.CNT 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 107 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:37310 CAPLUS

DN 138:237347

TI Transcription profiling in rat liver in response to dietary docosahexaenoic acid implicates stearyl-coenzyme A desaturase as a nutritional target for lipid lowering

AU Kramer, Jeffrey A.; LeDeaux, John; Butteiger, Dustie; Young, Tracy; Crankshaw, Carolyn; Harlow, Harry; Kier, Larry; Bhat, B. Ganesh

CS Nutrition and Consumer Sector, Pharmacia Corporation, St. Louis, MO, 63167, USA

SO Journal of Nutrition (2003), 133(1), 57-66 CODEN: JONUAI; ISSN: 0022-3166

PB American Society for Nutritional Sciences

DT Journal

LA English

AB The \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* in response to dietary docosahexaenoic acid rich oil for 6 wk was analyzed in the livers of male Sprague-Dawley rats to identify genes whose expression was regulated by dietary modification and \*\*\*correlated\*\*\* with serum lipid changes. Such genes may represent targets for intervention into cardiovascular health using nutraceuticals. High d. glass microarrays contg. .apprx.7800 cloned expressed sequences from rat were used to identify those genes that responded to dietary long chain (n-3) fatty acids. In general, dietary long chain (n-3) fatty acids exhibited statistically significant lipid-lowering effects similar to a pharmaceutical alternative, fenofibrate, but showed narrower effects on the transcription of most of the genes \*\*\*assayed\*\*\*. The transcription patterns confirmed that the expression of several key genes involved in cholesterol metab., fatty acid .beta.-oxidn. and lipogenesis was affected. These analyses indicated that stearyl-CoA (.DELTA.9) desaturase, a key enzyme involved in the regulation of triglyceride biosynthesis and

secretion, is a potential target for nutritional intervention for hyperlipidemia and cardiovascular health. In addn. these results suggested that regulation of the farnesoid X receptor may be a key nutritionally regulated mediator of serum lipid changes. A nutritional product concept based on a convenient dietary aid demonstrated comparable efficacy with less spurious gene regulation than a pharmaceutical alternative.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 108 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:29507 CAPLUS

DN 138:84442

TI Screening regulators of visceral fat accumulation by microarray \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* analysis

IN Matsuki, Yasushi; Iguchi, Haruhisa

PA Sumitomo Chemical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 34 pp. CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI	JP 2003009900	A2	20030114	JP 2001-198641
	20010629			

PRAI	JP 2001-198641		20010629	
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AB An anal. method is provided for screening compds. that promote or inhibit the accumulation of adipose tissue inside abdominal cavity based on measurement of expression level of multiple genes listed in tables herein enclosed. Expression level of those genes are measured in visceral fat cells upon exposure to the \*\*\*test\*\*\* compds. or in absence using DNA microarrays (gene chips). In this method, the adipose tissue quantity inside abdominal cavity is \*\*\*correlated\*\*\* with the expression level of certain gene(s) whose expression level was found to be affected by exposure to 17.beta. estradiol. Based on the measurement of expression level of multiple genes in rat adipose cells, activity of 17.beta. estradiol for inhibiting visceral fat accumulation was calcd. to be 95%, while that of estron was calcd. to be 94%.

L9 ANSWER 109 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:23562 CAPLUS

DN 138:67829

TI A relational database system and method for retrieving and using gene expression data from multiple sources

IN Markowitz, Victor; Topaloglou, Thodoros; Chen, I-Min Amy

PA USA

SO U.S. Pat. Appl. Publ., 47 pp. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI	US 2003009295	A1	20030109	US 2002-96645
	20020314			

PRAI	US 2001-275465P	P	20010314	
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AB A database system that can be used to store, manage, and analyze gene expression data is described. The system includes a gene expression database for storing quant. gene expression measurements for tissues and cell lines screened using various \*\*\*assays\*\*\*; a clin. database for storing information on bio-

samples and donors; and a fragment index for biol. properties for DNA fragments. The databases are connected by a bus system that allows the loading of various types of data including gene annotation and sample information. The databases can be queried with a single interface and results from searching these databases can be \*\*\*correlated\*\*\*

L9 ANSWER 110 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:18944 CAPLUS

DN 138:232436

TI A systematic approach to reconstructing transcription networks in *Saccharomyces cerevisiae*

AU Wang, Wei; Cherry, J. Michael; Botstein, David; Li, Hao  
CS Department of Genetics, Stanford University, Stanford, CA, 94305-5120, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(26), 16893-16898 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Decompg. regulatory networks into functional modules is a first step toward deciphering the logical structure of complex networks. We propose a systematic approach to reconstructing transcription modules (defined by a transcription factor and its target genes) and identifying conditions/perturbations under which a particular transcription module is activated/deactivated. Our approach integrates information from regulatory sequences, genome-wide mRNA expression data, and functional annotation. We systematically analyzed \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* expts. in which the yeast cell was subjected to various environmental or genetic perturbations. We were able to construct transcription modules with high specificity and sensitivity for many transcription factors, and predict the activation of these modules under anticipated as well as unexpected conditions. These findings generate \*\*\*testable\*\*\* hypotheses when combined with existing knowledge on signaling pathways and protein-protein interactions. \*\*\*Correlating\*\*\* the activation of a module to a specific perturbation predicts links in the cell's regulatory networks, and examg. coactivated modules suggests specific instances of crosstalk between regulatory pathways.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 111 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:9873 CAPLUS

DN 138:266690

TI Replicate high-density rat genome oligonucleotide microarrays reveal hundreds of regulated genes in the dorsal root ganglion after peripheral nerve injury

AU Costigan, Michael; Befort, Katia; Karchewski, Laurie; Griffin, Robert S.; D'Urso, Donatella; Allchorne, Andrew; Sitarski, Joanne; Mannion, James W.; Pratt, Richard E.; Woolf, Clifford J.

CS Department of Anesthesia and Critical Care, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, 02129, USA

SO BMC Neuroscience [online computer file] (2002), 3, No pp. given CODEN: BNMEA6; ISSN: 1471-2202 URL: <http://www.biomedcentral.com/1471-2202/3/16>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Background: Rat oligonucleotide microarrays were used to detect changes in gene expression in the dorsal root ganglion (DRG) 3 days following sciatic nerve transection (axotomy). Two comparisons were made using two sets of triplicate microarrays, naive vs. naive and naive vs. axotomy. Results: Microarray variability was assessed using the naive vs. naive comparison. These results support use of a  $P < 0.05$  significance threshold for detecting regulated genes, despite the large no. of hypothesis \*\*\*tests\*\*\* required. For the naive vs. axotomy comparison, a 2-fold cut off alone led to an estd. error rate of 16%; combining a  $> 1.5$ -fold expression change and  $P < 0.05$  significance reduced the estd. error to 5%. The 2-fold cut off identified 178 genes while the combined  $>1.5$ -fold and  $P < 0.05$  criteria generated 240 putatively regulated genes, which we have listed. Many of these have not been described as regulated in the DRG by axotomy. Northern blot, quant. slot blots and in situ hybridization verified the expression of 24 transcripts. These data showed an 83% concordance rate with the arrays; most mismatches represent genes with low expression levels reflecting limits of array sensitivity. A significant \*\*\*correlation\*\*\* was found between actual mRNA differences and relative changes between microarrays ( $R^2 = 0.8567$ ). Temporal patterns of individual genes regulation varied. Conclusions: We identify parameters for microarray anal. which reduce error while identifying many putatively regulated genes. Functional classification of these genes suggest reorganization of cell structural components, activation of genes expressed by immune and inflammatory cells and down-regulation of genes involved in neurotransmission.

RE.CNT 139 THERE ARE 139 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 112 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:5335 CAPLUS

DN 138:53907

TI Marker genes for identification, assessment, prevention, and therapy of ovarian cancer

IN Kovats, Steven G.; Sen, Ami; Morrissey, Michael P.; Lillie, James

PA Millennium Pharmaceuticals, Inc., USA

SO U.S. Pat. Appl. Publ., 47 pp. CODEN: USXXCO

DT Patent

LA English

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE				
PI	US 2003003479	A1	20030102	US 2002-126227	
	20020419				
PRAI	US 2001-285443P	P	20010419		

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers. A variety of marker genes are provided, wherein changes in the levels of expression of one or more of the marker genes is \*\*\*correlated\*\*\* with the presence of ovarian cancer.

L9 ANSWER 113 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:3894 CAPLUS

DN 138:199477

TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* of isogenic cells with different TP53 gene dosage reveals numerous genes that are affected by TP53 dosage and identifies CSPG2 as a direct target of p53

AU Yoon, Heejei; Liyanarachchi, Sandya; Wright, Fred A.; Davuluri, Ramana; Lockman, Janet C.; De la Chapelle, Albert; Pellegata, Natalia S.

CS Human Cancer Genetics Program, Comprehensive Cancer Center, Ohio State University, Columbus, OH, 43210, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(24), 15632-15637 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB TP53 does not fully comply with the Knudson model in that a redn. of constitutional expression of p53 may be sufficient for tumor predisposition. This finding suggests a gene-dosage effect for p53 function. To det. whether TP53 gene dosage affects the transcriptional regulation of target genes, we performed oligonucleotide-array gene expression anal. by using human cells with wild-type p53 (p53 +/+), or with one (p53 +/-), or both (p53 -/-) TP53 alleles disrupted by homologous recombination. We identified 35 genes whose expression is significantly \*\*\*correlated\*\*\* to the dosage of TP53. These genes are involved in a variety of cellular processes including signal transduction, cell adhesion, and transcription regulation. Several of them are involved in neurogenesis and neural crest migration, developmental processes in which p53 is known to play a role. Motif search anal. revealed that of the genes highly expressed in p53 +/+ and +/- cells, several contain a putative p53 consensus binding site (bs), suggesting that they could be directly regulated by p53. Among those genes, we chose CSPG2 (which encodes versican) for further study because it contains a bona fide p53 bs in its first intron and its expression highly \*\*\*correlates\*\*\* with TP53 dosage. By using in vitro and in vivo \*\*\*assays\*\*\*, we showed CSPG2 to be directly transactivated by p53. In conclusion, we developed a strategy to demonstrate that many genes are affected by TP53 gene dosage for their expression. We report several candidate genes as potential downstream targets of p53 in nonstressed cells. Among them, CSPG2 is validated as being directly transactivated by p53. Our method provides a useful tool to elucidate addnl. mechanisms by which p53 exerts its functions.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 114 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:983913 CAPLUS

DN 138:235764

TI Identifying distinct classes of bladder carcinoma using microarrays

AU Dyrskjot, Lars; Thykjaer, Thomas; Kruhoffer, Mogens; Jensen, Jens Ledet; Marcussen, Niels; Hamilton-Dutoit, Stephen; Wolf, Hans; Orntoft, Torben F.

CS Department of Clinical Biochemistry, Molecular Diagnostic Laboratory, Aarhus University Hospital, Skejby, Aarhus, DK-8200, Den.

SO Nature Genetics (2003), 33(1), 90-96 CODEN: NGENEC; ISSN: 1061-4036

PB Nature Publishing Group

DT Journal

LA English

AB Bladder cancer is a common malignant disease characterized by frequent recurrences. The stage of disease at diagnosis and the presence of surrounding carcinoma in situ are important in detg. the disease course of an affected individual. Despite considerable effort, no accepted immunohistol. or mol. markers

have been identified to define clin. relevant subsets of bladder cancer. Here we report the identification of clin. relevant subclasses of bladder carcinoma using expression microarray anal. of 40 well characterized bladder tumors. Hierarchical cluster anal. identified three major stages, Ta, T1 and T2-4, with the Ta tumors further classified into subgroups. We built a 32-gene mol. classifier using a cross-validation approach that was able to classify benign and muscle-invasive tumors with close \*\*\*correlation\*\*\* to pathol. staging in an independent \*\*\*test\*\*\* set of 68 tumors. The classifier provided new predictive information on disease progression in Ta tumors compared with conventional staging ( $P < 0.005$ ). To delineate non-recurring Ta tumors from frequently recurring Ta tumors, we analyzed expression patterns in 31 tumors by applying a supervised learning classification methodol., which classified 75% of the samples correctly ( $P < 0.006$ ). Furthermore, \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* characterizing each stage and subtype identified their biol. properties, producing new potential targets for therapy. RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 115 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:978087 CAPLUS

DN 138:53906

TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* for diagnosis of breast cancer patients and classification based on estrogen receptor and BRCA1 and prognosis

IN Dai, Hongyue; He, Yudong; Linsley, Peter S.; Mao, Mao; Roberts, Christopher J.; Van't Veer, Laura Johanna; Van de Vijver, Marc J.; Bernards, Rene; Hart, A. A. M.

PA Rosetta Inpharmatics, Inc., USA

SO PCT Int. Appl., 187 pp. CODEN: PIXXD2

DT Patent

LA	English	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	----	-----	-----

PI WO 2002103320 A2 20021227 WO 2002-US18947 20020614 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR PRAI US 2001-2001/PV29891U 20010618 US 2002-2002/PV380710 20020514

AB The present invention relates to genetic markers whose expression is \*\*\*correlated\*\*\* with breast cancer. Specifically, the invention provides sets of markers whose expression patterns can be used to differentiate clin. conditions assocd. with breast cancer, such as the presence or absence of the estrogen receptor ESR1, and BRCA1 and sporadic tumors, and to provide information on the likelihood of tumor distant metastases within five years of initial diagnosis. The invention relates to methods of using these markers to distinguish these conditions. The invention also relates to kits contg. ready-to-use microarrays and computer software for data anal. using the statistical methods disclosed herein.

L9 ANSWER 116 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:968514 CAPLUS  
DN 138:249211

TI Guiding revision of regulatory models with expression data  
AU Shrager, Jeff; Langley, Pat; Pohorille, Andrew  
CS Institute for the Study of Learning and Expertise, Palo Alto, CA, 94306, USA  
SO Pacific Symposium on Biocomputing 2002, Kauai, HI, United States, Jan. 3-7, 2002 (2001), 486-497. Editor(s): Altman, Russ B. Publisher: World Scientific Publishing Co. Pte. Ltd., Singapore, Singapore. CODEN: 69DJST; ISBN: 981-02-4777-X  
DT Conference  
LA English

AB BioLingua is a computational system designed to support biologists' efforts to construct models, make predictions, and interpret data. In this paper, we focus on the specific task of revising an initial model of gene regulation based on expression levels from gene microarrays. We describe BioLingua's formalism for representing process models, its method for predicting qual. \*\*\*correlations\*\*\* from such models, and its use of data to constrain search through the space of revised models. We also report exptl. results on revising a model of photosynthetic regulation in Cyanobacteria to better fit expression data for both wild and mutant strains, along with model mutilation studies designed to \*\*\*test\*\*\* our method's robustness. In closing, we discuss related work on representing, discovering, and revising biol. models, after which we propose some directions for future research.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 117 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:961392 CAPLUS  
DN 139:239779

TI Gene therapy for prostate cancer: toxicological profile of four HSV-tk transducing adenoviral vectors regulated by different promoters

AU Ebara, S.; Shimura, S.; Nasu, Y.; Kaku, H.; Kumon, H.; Yang, G.; Wang, J.; Timme, T. L.; Aguilar-Cordova, E.; Thompson, T. C.

CS Scott Department of Urology, Baylor College of Medicine, Houston, TX, USA

SO Prostate Cancer and Prostatic Diseases (2002), 5(4), 316-325 CODEN: PCPDFW; ISSN: 1365-7852

PB Nature Publishing Group

DT Journal

LA English

AB Adenoviral vector delivery of the Herpes simplex virus thymidine kinase (HSV-tk) gene in combination with the prodrug ganciclovir (GCV) has been \*\*\*tested\*\*\* in phase I clin. trials for prostate cancer and found to exhibit a satisfactory toxicity profile. We have developed addnl. adenoviral vectors with differing promoters to optimize the \*\*\*expression\*\*\* \*\*\*profile\*\*\* and in the present study evaluate the potential systemic toxicity of these vectors. Four recombinant adenoviral vectors that express the HSV-tk gene were generated using three different promoters: CMV (leftward orientation); RSV (both rightward and leftward orientation); and the mouse caveolin-1 (cav-1) promoter (leftward orientation). Efficacy was detd. in vitro by cytotoxicity \*\*\*assays\*\*\* in a mouse prostate cancer cell line, RM-9, and in vivo by treating orthotopic tumors. Potential toxicity was evaluated from liver histol. and apoptotic cell counts and enzyme levels in the serum following i.v. adenoviral vector injection. Although there were differences in HSV-tk expression at the protein level among the four vectors

there were no significant differences in in-vitro cytotoxicity studies with GCV or in vivo in tumor growth suppression of an orthotopic mouse prostate cancer model in GCV treated mice. I.v. delivery of high doses of all adenoviral vectors lead to abnormalities in liver function as measured by specific serum markers and histol. evaluation of liver tissue and increased levels of apoptosis in the liver. These abnormalities were most prevalent with the vector contg. the CMV promoter and the rightward oriented RSV promoter. They were least prevalent in the vector regulated by the cav-1 promoter. Upregulation of specific chemokines, MIP-2 and MIP-1.beta. was \*\*\*correlated\*\*\* with apoptotic counts. Our results demonstrate that comprehensive toxicol. anal. of adenoviral vectors provides internally consistent information that can differentiate vectors with comparable efficacy based on toxicity. In these studies vectors with the cav-1 promoter-driven and leftward RSV-driven HSV-tk gene demonstrated minimal toxicities with cytotoxic effectiveness comparable to more toxic vectors. Our studies further suggest that promoter selection can influence the toxic effects of an adenoviral gene therapy vector.  
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 118 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:894177 CAPLUS  
DN 138:181921

TI Gene clustering based on RNAi phenotypes of ovary-enriched genes in C. elegans

AU Piano, Fabio; Schetter, Aaron J.; Morton, Diane G.; Gunsalus, Kristin C.; Reinke, Valerie; Kim, Stuart K.; Kemphues, Kenneth J.

CS Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, 14853, USA

SO Current Biology (2002), 12(22), 1959-1964 CODEN: CUBLE2; ISSN: 0960-9822

PB Cell Press

DT Journal

LA English

AB Recently, a set of 766 genes with enriched expression in the ovary as compared to the soma was identified by microarray anal. . Here, we report a functional anal. of 98% of these genes by RNA interference (RNAi). Over half the genes \*\*\*tested\*\*\* showed at least one detectable phenotype, most commonly embryonic lethality, consistent with the expectation that ovary transcripts would be enriched for genes that are essential in basic cellular and developmental processes. We find that essential genes are more likely to be conserved and to be highly expressed in the ovary. We extend previous observations and find that fewer than the expected no. of ovary-expressed essential genes are present on the X chromosome. We characterized early embryonic defects for 161 genes and used time-lapse microscopy to systematically describe the defects for each gene in terms of 47 RNAi-assocd. phenotypes. In this paper, we discuss the use of these data to group genes into "phenoclusters"; in the accompanying paper, we use these data as one component in the integration of different types of large-scale functional analyses . We find that phenoclusters \*\*\*correlate\*\*\* well with sequence-based functional predictions and thus may be useful in predicting functions of uncharacterized genes.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 119 OF 169 CAPLUS COPYRIGHT 2005 ACS on  
STN

AN 2002:832566 CAPLUS

DN 137:334078

TI Human genes differentially expressed in breast cancer  
tissues and their use for identification, assessment, prevention,  
and therapy of breast cancer

IN Lillie, James; Palermo, Adam; Wang, Youzhen; Steinmann,  
Kathleen; Elias, Josh; Mertens, Maureen

PA Millennium Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 725 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI WO 2002085298 A2 20021031 WO 2002-US12612  
20020419 WO 2002085298 A3 20030522 W: AE, AG,  
AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,  
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM,  
ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM,  
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
TD, TG US 2003215805 A1 20031120 US 2002-125968  
20020419

PRAI US 2001-285163P P 20010420

AB The invention relates newly discovered \*\*\*correlations\*\*\*  
between expression of certain human marker genes and the  
cancer state of breast cells. The level of expression of individual  
marker genes and combinations of marker genes  
\*\*\*correlates\*\*\* with the presence of breast cancer or a pre-  
malignant condition in a patient. Thus, 1417 gene sequences  
assocd. with breast cancer are discovered in PCR-based  
subtracted cDNA libraries and by in situ hybridization. Methods  
are provided for detecting the presence of breast cancer in a  
sample, the absence of breast cancer in a sample, the stage of a  
breast cancer, the metastatic potential of a breast cancer, the  
indolence or aggressiveness of the cancer, and other  
characteristics of breast cancer that are relevant to prevention,  
diagnosis, characterization and therapy of breast cancer in a  
patient.

L9 ANSWER 120 OF 169 CAPLUS COPYRIGHT 2005 ACS on  
STN

AN 2002:809899 CAPLUS

DN 138:53853

TI Cyr61 and CTGF are molecular markers of bladder wall  
remodeling after outlet obstruction

AU Chaqour, Brahim; Whitbeck, Catherine; Han, Ji-Soo;  
Macarak, Edward; Horan, Pat; Chichester, Paul; Levin, Robert  
CS Dept of Anatomy and Histology, University of Pennsylvania,  
Philadelphia, PA, 19104, USA

SO American Journal of Physiology (2002), 283(4, Pt. 1), E765-  
E774 CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal

LA English

AB Cysteine-rich protein (Cyr61) and connective tissue growth  
factor (CTGF) are key immediate early growth factors with  
functions in cell proliferation, differentiation, and extracellular  
matrix synthesis. Studies were performed to assess the

\*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* of Cyr61  
and CTGF in rat urinary bladder during growth in response to  
partial outlet obstruction. The mRNA levels of Cyr61 as detd. by  
RNase protection \*\*\*assay\*\*\* increased sharply after 1 day  
and remained elevated throughout the time period of the  
obstruction. This \*\*\*correlates\*\*\* well with increased  
bladder wt. The CTGF mRNA levels seemed to peak within the  
second week of the urethral obstruction and \*\*\*correlate\*\*\*  
well with increased type I collagen mRNA. The expression  
pattern of either Cyr61 or CTGF proteins corroborated that of  
their resp. mRNAs. Immunohistochem. analyses showed that  
immunoreactivity of Cyr61 was confined to detrusor smooth  
muscle and that of CTGF was detected within both detrusor  
muscle and lamina propria layers. These data strongly indicate  
the involvement of Cyr61 and CTGF in bladder wall remodeling as  
a result of the outlet obstruction.

RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 121 OF 169 CAPLUS COPYRIGHT 2005 ACS on  
STN

AN 2002:806370 CAPLUS

TI Inferring domain-domain interactions from protein-protein  
interactions

AU Deng, Minghua; Mehta, Shipra; Sun, Fengzhu; Chen, Ting  
CS Program in Molecular and Computational Biology,  
Department of Biological Sciences, University of Southern  
California, Los Angeles, CA, 90089, USA

SO Genome Research (2002), 12(10), 1540-1548 CODEN:  
GEREFS; ISSN: 1088-9051

PB Cold Spring Harbor Laboratory Press

DT Journal; Letter

LA English

AB The interaction between proteins is one of the most  
important features of protein functions. Behind protein-protein  
interactions there are protein domains interacting phys. with one  
another to perform the necessary functions. Therefore,  
understanding protein interactions at the domain level gives a  
global view of the protein interaction network, and possibly of  
protein functions. Two research groups used yeast two-hybrid  
\*\*\*assays\*\*\* to generate 5719 interactions between proteins  
of the yeast *Saccharomyces cerevisiae*. This allows us to study  
the large-scale conserved patterns of interactions between  
protein domains. Using evolutionarily conserved domains defined  
in a protein-domain database called PFAM, we apply a Maximum  
Likelihood Estn. method to infer interacting domains that are  
consistent with the obsd. protein-protein interactions. We est.  
the probabilities of interactions between every pair of domains  
and measure the accuracies of our predictions at the protein  
level. Using the inferred domain-domain interactions, we predict  
interactions between proteins. Our predicted protein-protein  
interactions have a significant overlap with the protein-protein  
interactions obtained by methods other than the two-hybrid  
\*\*\*assays\*\*\*. The mean \*\*\*correlation\*\*\* coeff. of the  
\*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* for our  
predicted interaction pairs is significantly higher than that for  
random pairs. Our method has shown robustness in analyzing  
incomplete data sets and dealing with various exptl. errors. We  
found several novel protein-protein interactions such as RPSOA  
interacting with APG17 and TAF40 interacting with SPT3, which  
are consistent with the functions of the proteins.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 122 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:795868 CAPLUS

DN 138:101547

TI Use of RNA and genomic DNA references for inferred comparisons in DNA microarray analyses

AU Kim, H.; Zhao, B.; Snesrud, E. C.; Haas, B. J.; Town, C. D.; Quackenbush, J.

CS The Institute for Genomic Research, Rockville, MD, USA  
SO BioTechniques (2002), 33(4), 924-930 CODEN: BTNQDO; ISSN: 0736-6205

PB Eaton Publishing Co.

DT Journal

LA English

AB In most microarray \*\*\*assays\*\*\*, labeled cDNA mols. derived from ref. and query RNA samples are co-hybridized to probes arrayed on a glass surface. \*\*\*Gene\*\*\*

\*\*\*expression\*\*\* \*\*\*profiles\*\*\* are then calcd. for each gene based on the relative hybridization intensities measured between the two samples. The most commonly used ref. samples are typically isolates from a single representative RNA source (RNA-O) or pooled mixts. of RNA derived from a plurality of sources (RNA-p). Genomic DNA offers an alternative ref. nucleic acid with a no. of potential advantages, including stability, reproducibility, and a potentially uniform representation of all genes, as each unique gene should have equal representation in a haploid genome. Using hydrogen peroxide-treated Arabidopsis thaliana plants as a model, we evaluated genomic DNA and RNA-p as ref. samples and compared expression levels inferred through the ref. relative to unexposed plants with expression levels measured directly using an RNA-O ref. Our anal. demonstrates that while genomic DNA can serve as a reasonable ref. source for microarray \*\*\*assays\*\*\*, a much greater \*\*\*correlation\*\*\* with direct measurements can be achieved using an RNA-based ref. sample.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 123 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:783124 CAPLUS

DN 138:101264

TI Neuropeptide AF and FF modulation of adipocyte metabolism. Primary insights from functional genomics and effects on .beta.-adrenergic responsiveness

AU Lefrere, Isabelle; de Coppet, Pierre; Camelin, Jean-Claude; Le Lay, Soazig; Mercier, Nathalie; Elshourbagy, Nabil; Bril, Antoine; Berrebi-Bertrand, Isabelle; Feve, Bruno; Krief, Stephane

CS GlaxoSmithKline Laboratoires Pharmaceutiques, Saint-Gregoire, 35762, Fr.

SO Journal of Biological Chemistry (2002), 277(42), 39169-39178 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB The presence of a neuropeptide AF and FF receptor (NPFF-R2) mRNA in human adipose tissue suggested these peptides, principally recognized for their pain modulating effects, may also impact on adipocyte metab., an aspect that has not been explored previously. The authors' aim was thus to obtain more insights into the actions of these peptides on adipocytes, an approach initially undertaken with a functional genomic \*\*\*assay\*\*\*. First the authors showed that 3T3-L1 adipocytes express both NPFF-R1 and NPFF-R2 transcripts, and that NPAF binds adipocyte membranes with a nanomolar affinity as

assessed by surface plasmon resonance technol. Then, and following a 24-h treatment with NPFF or NPAF (1 .mu.M), the authors have measured using real-time quant. reverse transcriptase-PCR the mRNA steady state levels of already well characterized genes involved in key pathways of adipose metab. Among the 45 genes \*\*\*tested\*\*\*, few were modulated by NPFF (.apprx.10%) and a larger no. by NPAF (.apprx.27%). Interestingly, NPAF increased the mRNA levels of .beta.2- and .beta.3-adrenergic receptors (AR), and to a lesser extent those of .beta.1-ARs. These variations in catecholamine receptor mRNAs \*\*\*correlated\*\*\* with a clear induction in the d. of .beta.2- and .beta.3-AR proteins, and in the potency of .beta.-AR subtype-selective agonists to stimulate adenylyl cyclase activity. Altogether, these data show that NPFF-R1 and NPFF-R2 are functionally present in adipocytes and suggest that besides their well described pain modulation effects, NPAF and to a lesser extent NPFF, may have a global impact on body energy storage and utilization.

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 124 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:781127 CAPLUS

DN 137:293324

TI Postremission therapy with low-dose interleukin 2 with or without intermediate pulse dose interleukin 2 therapy is well tolerated in elderly patients with acute myeloid leukemia: cancer and leukemia group B study 9420

AU Farag, Sherif S.; George, Stephen L.; Lee, Edward J.; Baer, Maria; Dodge, Richard K.; Becknell, Brian; Fehniger, Todd; Silverman, Lewis R.; Crawford, Jeffrey; Bloomfield, Clara D.; Larson, Richard A.; Schiffer, Charles A.; Caligiuri, Michael A.  
CS The Ohio State University Comprehensive Cancer Center, Columbus, OH, 43210, USA

SO Clinical Cancer Research (2002), 8(9), 2812-2819 CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB The purpose of the study is to investigate the tolerability of interleukin 2 (IL-2) after intensive chemotherapy in elderly acute myeloid leukemia (AML) patients in first complete remission (CR). AML patients .gtoreq.60 yr in CR after induction and consolidation chemotherapy on Cancer and Leukemia Group B study 9420 were eligible if they had neutrophils .gtoreq.1 .times. 10<sup>9</sup>/L and platelets .gtoreq.75 .times. 10<sup>9</sup>/L. Patients received low-dose IL-2 (1 .times. 10<sup>6</sup> IU/m<sup>2</sup>/day s.c. for 90 days) or low-dose IL-2 with intermediate pulse doses (6-12 .times. 10<sup>6</sup> IU/m<sup>2</sup>/day s.c. for 3 days) every 14 days (max. five pulses). In a subset of patients, we investigated the expression of NKG2D ligands by leukemic cells because they are likely important mediators of natural killer cytotoxicity. Of 35 CR patients receiving IL-2, 34 were evaluable for toxicity. Median age was 67 (range, 60-76) years. Thirteen of 16 patients receiving low-dose IL-2 completed the planned therapy, and 11 of 18 who also received intermediate pulse dose IL-2 therapy completed all five pulses. The spectrum of toxicity in both groups was similar, with predominantly grade 1-2 fatigue, fever, injection site reactions, nausea, anemia, and thrombocytopenia. Grade 3-4 hematol. and nonhematol. toxicity were more frequent in patients also receiving intermediate pulse dose IL-2 therapy. Grade 3-4 fatigue and hematol. toxicity, although uncommon, were the major causes for discontinuing or attenuating therapy. In 8 cases, mRNA for one or more NKG2D ligands was detected in



leukemic cells obtained at diagnosis before treatment. Low-dose IL-2, with or without intermediate pulse dose therapy, given immediately after chemotherapy in first CR to elderly AML patients is well tolerated. Expression of NKG2D ligands by leukemic cells was detected in the majority of cases  
\*\*\*tested\*\*\* and should be assessed for \*\*\*correlation\*\*\* with response to IL-2 in future studies.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 125 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:779634 CAPLUS

DN 138:36954

TI Expression of interleukin 8 and not parathyroid hormone-related protein by human breast cancer cells \*\*\*correlates\*\*\* with bone metastasis in vivo

AU Bendre, Manali S.; Gaddy-Kurten, Dana; Mon-Foote, Thetsu; Akel, Nisreen S.; Skinner, Robert A.; Nicholas, Richard W.; Suva, Larry J.

CS Center for Orthopaedic Research, Departments of Orthopaedic Surgery and Physiology and Biophysics, Barton Research Institute, University of Arkansas for Medical Sciences, Little Rock, AR, 72205, USA

SO Cancer Research (2002), 62(19), 5571-5579 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB Metastasis is the process by which tumor cells spread from their site of origin to distant sites after gaining access to the circulatory system. An understanding of the factors contributing to the metastatic potential of breast cancer cells to bone will enhance the prospect of developing new therapies that impede metastasis. In this study, we have used an in vivo selection scheme involving left cardiac ventricle injection into nude mice to identify a highly metastatic human breast cancer cell line (MDA-MET) from a less metastatic (MDA-231) parental cell line. In this model, tumor-bearing mice exhibit features similar to those assocd. with human metastatic bone disease such as osteolytic bone destruction. After inoculation, MDA-MET cells form devastating lesions within 4 wk, whereas the parental cells do not, even after 10 wk. In vitro, the MDA-MET cells have a similar growth rate to the parental MDA-231 cells yet demonstrate distinct adhesive and invasive phenotypes. MDA-MET cells show increased early adhesion to type IV collagen and are significantly more invasive through Matrigel than MDA-231 cells. Anal. of the \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* in the metastatic MDA-MET vs. poorly metastatic MDA-231 cells identified relatively few genes whose expression was altered >2-fold. Of particular interest was the lack of parathyroid hormone-related protein (PTHrP) mRNA expression, which was supported at the protein level by immunoradiometric \*\*\*assay\*\*\*. These data support the idea that PTHrP is not predictive of the metastasis of human breast cancer to bone. Another important difference between the two cell lines was the elevated expression by MDA-MET cells of the cytokine IL-8. Reverse transcriptase-PCR and ELISA confirmed the increased expression of IL-8 in MDA-MET cells. In addn., IL-8 mRNA expression is also elevated in a variety of human cancer cell lines with different metastatic potential in vivo. These expts. suggest that the elevated expression of IL-8 (and not PTHrP) by MDA-MET cells is a phenotypic change that may be related to their enhanced ability to metastasize to the skeleton.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 126 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:772513 CAPLUS

DN 138:118255

TI \*\*\*Expression\*\*\* \*\*\*profiling\*\*\* of Drosophila imaginal discs

AU Klebes, Ansgar; Biehs, Brian; Cifuentes, Francisco; Kornberg, Thomas B.

CS Department of Biochemistry and Biophysics, University of California, San Francisco, CA, 94143, USA

SO GenomeBiology [online computer file] (2002), 3(8), No pp. given CODEN: GNBLFW; ISSN: 1465-6914 URL: <http://www.genomebiology.com/content/pdf/gb-2002-3-8-research0038.pdf>

PB BioMed Central Ltd.

DT Journal; (online computer file)

LA English

AB Background: In the Drosophila larva, imaginal disks are programmed to produce adult structures at metamorphosis. Although their fate is precisely detd., these organs remain largely undifferentiated in the larva. To identify genes that establish and express the different states of detn. in disks and larval tissues, we used DNA microarrays to analyze mRNAs isolated from single imaginal disks. Results: Linear amplification protocols were used to generate hybridization probes for microarray anal. from poly(A)+ RNA from single imaginal disks contg. between 10,000 and 60,000 cells. Probe reproducibility and degree of representation were \*\*\*tested\*\*\* using microarrays with approx. 6,000 different cDNAs. Hybridizations with probes that had been prepd. sep. from the same starting RNA pool had a \*\*\*correlation\*\*\* coeff. of 0.97. \*\*\*Expression\*\*\* \*\*\*profile\*\*\* comparisons of the left and right wing imaginal disks from the same larva \*\*\*correlated\*\*\* with a coeff. of 0.99, indicating a high degree of reproducibility of independent amplifications. Using this method, we identified genes with preferential expression in the different imaginal disks using pairwise comparisons of disks and larval organs. Whereas disk-to-disk comparisons revealed only moderate differences, profiles differed substantially between imaginal disks and larval tissues, such as larval endodermal midgut and mesodermal fat body. Conclusion: The combination of linear RNA amplification and DNA microarray hybridization allowed us to det. the \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of individual imaginal disks and larval tissues and to identify \*\*\*genes\*\*\* \*\*\*expressed\*\*\* in tissue-specific \*\*\*patterns\*\*\*. These methods should be widely applicable to comparisons of \*\*\*expression\*\*\* \*\*\*profiles\*\*\* for tissues or parts of tissues that are available only in small amts.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 127 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:760161 CAPLUS

DN 138:235382

TI Expression of a novel HsMCAK mRNA splice variant, tsMCAK gene, in human \*\*\*testis\*\*\*

AU Cheng, Li Jun; Zhou, Zuo Min; Li, Jian Min; Zhu, Hui; Zhu, Hu; Zhou, Ya Dong; Wang, Li Rong; Lin, Min; Sha, Jia Hao

CS Center of Human Functional Genomics, Key Laboratory of Reproductive Medicine, Nanjing Medical University, Nanjing, Jiangsu Province, 210029, Peop. Rep. China  
SO Life Sciences (2002), 71(23), 2741-2757 CODEN: LIFSAK; ISSN: 0024-3205

PB Elsevier Science Inc.

DT Journal

LA English

AB Identification of specifically expressed genes in the adult or fetal **\*\*\*testis\*\*\*** is very important for the study of genes related to the development and function of the **\*\*\*testis\*\*\***. In this study, a human adult **\*\*\*testis\*\*\*** cDNA microarray was constructed and hybridized with 33P-labeled human adult and embryo **\*\*\*testis\*\*\*** cDNA probes, resp. After differential display analyzing, a no. of new genes related to the development of **\*\*\*testis\*\*\*** and spermatogenesis had been identified. One of these new genes is tsMCAK. tsMCAK was expressed 2.62 folds more in human adult **\*\*\*testis\*\*\*** than fetal **\*\*\*testis\*\*\***. The full length of tsMCAK is 2401 bp and contains a 2013 bp open reading frame, encoding a 671-amino-acid protein. Sequence anal. showed that it has a central kinesin motor domain and is homologous to HsMCAK gene of the somatic cells. Blasting human genome database localized tsMCAK to human chromosome 1P34 and further investigation showed that it is a splice variant of HsMCAK. The tissue distribution of tsMCAK was detd. by RT-PCR and it is expressed highly and specifically in the **\*\*\*testis\*\*\***. Southern blot studies of its expression in patients with infertility indicated its specific expression in spermatogenic cells and its **\*\*\*correlation\*\*\*** with male infertility. The above results suggested that tsMCAK is a candidate gene for the **\*\*\*testis\*\*\***-specific KRPs and its specific expression in the **\*\*\*testis\*\*\*** was **\*\*\*correlated\*\*\*** with spermatogenesis and may be **\*\*\*correlated\*\*\*** with male infertility.  
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 128 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:715770 CAPLUS

DN 138:20269

TI GeneChip expression analysis of the iron starvation response in *Pseudomonas aeruginosa*: identification of novel pyoverdine biosynthesis genes

AU Ochsner, Urs A.; Wilderman, Paula J.; Vasil, Adriana I.; Vasil, Michael L.

CS Department of Microbiology, University of Colorado Health Sciences Center, Denver, CO, 80262, USA

SO Molecular Microbiology (2002), 45(5), 1277-1287 CODEN: MOMIEE; ISSN: 0950-382X

PB Blackwell Science Ltd.

DT Journal

LA English

AB Upon iron restriction, the opportunistic pathogen *Pseudomonas aeruginosa* produces various virulence factors, including siderophores, exotoxin, proteases and hemolysin. The ferric uptake regulator (Fur) plays a central role in this response and also controls other regulatory genes, such as pvdS, which encodes an alternative sigma factor. This circuit leads to a hierarchical cascade of direct and indirect iron regulation. We used the GeneChip to analyze the global **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** **\*\*\*profiles\*\*\*** in response to iron. In iron-starved cells, the expression of 118 genes was increased at least fivefold compared with that in iron-replete cells, whereas the expression of 87 genes was decreased at least fivefold. The GeneChip data **\*\*\*correlated\*\*\*** well with results obtained

using individual lacZ gene fusions. Strong iron regulation was obsd. for previously identified genes involved in biosynthesis or uptake of the siderophores pyoverdine and pyochelin, utilization of heterologous siderophores and heme and ferrous iron transport. A low-iron milieu led to increased expression of the genes encoding TonB, alk. protease, PrpL protease, exotoxin A, as well as fumarase C, Mn-dependent superoxide dismutase SodA, a ferredoxin and ferredoxin reductase and several oxidoreductases and dehydrogenases. Iron-controlled regulatory genes included seven alternative sigma factors and five other transcriptional regulators. Roughly 20% of the iron-regulated genes encoded proteins of unknown function and lacked any conclusive homologies. Under low-iron conditions, expression of 26 genes or operons was reduced in a .DELTA.pvdS mutant compared with wild type, including numerous novel pyoverdine biosynthetic genes. The GeneChip proved to be a very useful tool for rapid gene expression anal. and identification of novel genes controlled by Fur or PvdS.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 129 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:696982 CAPLUS

DN 137:349309

TI Heterologous array analysis in pinaceae: hybridization of Pinus taeda cDNA arrays with cDNA from needles and embryogenic cultures of P. taeda, P. sylvestris or Picea abies  
AU Van Zyl, Leonel; Von Arnold, Sara; Bozhkov, Peter; Chen, Yongzhong; Egertsdotter, Ulrika; MacKay, John; Sederoff, Ronald R.; Shen, Jing; Zelena, Lyubov; Clapham, David H.

CS Forest Biotechnology Group, North Carolina State University, Raleigh, NC, 27695, USA

SO Comparative and Functional Genomics (2002), 3(4), 306-318 CODEN: CFGOAT; ISSN: 1531-6912

PB John Wiley & Sons Ltd.

DT Journal

LA English

AB Hybridization of labeled cDNA from various cell types with high-d. arrays of expressed sequence tags is a powerful technique for investigating gene expression. Few conifer cDNA libraries have been sequenced. Because of the high level of sequence conservation between Pinus and Picea we have investigated the use of arrays from one genus for studies of gene expression in the other. The partial cDNAs from 384 identifiable genes expressed in differentiating xylem of Pinus taeda were printed on nylon membranes in randomized replicates. These were hybridized with labeled cDNA from needles or embryogenic cultures of Pinus taeda, P. sylvestris and Picea abies, and with labeled cDNA from leaves of Nicotiana tabacum. The Spearman **\*\*\*correlation\*\*\*** of gene expression for pairs of conifer species was high for needles ( $r_2 = 0.78 - 0.86$ ), and somewhat lower for embryogenic cultures ( $r_2 = 0.68 - 0.83$ ). The **\*\*\*correlation\*\*\*** of gene expression for tobacco leaves and needles of each of the three conifer species was lower but sufficiently high ( $r_2 = 0.52 - 0.63$ ) to suggest that many partial gene sequences are conserved in angiosperms and gymnosperms. Heterologous probing was further used to identify tissue-specific gene expression over species boundaries. To evaluate the significance of differences in gene expression, conventional parametric **\*\*\*tests\*\*\*** were compared with permutation **\*\*\*tests\*\*\*** after four methods of normalization. Permutation **\*\*\*tests\*\*\*** after Z-normalization provide the highest degree of discrimination but may enhance the probability of type I errors. It is concluded that arrays of cDNA from loblolly

pine are useful for studies of gene expression in other pines or spruces.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 130 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:641974 CAPLUS

DN 138:198259

TI Mechanisms of the growth inhibitory effects of the isoflavonoid biochanin A on LNCaP cells and xenografts  
AU Rice, Lori; Samed, Von G.; Medrano, Theresa A.; Sweeney, Carol A.; Baker, Henry V.; Stenstrom, Anne; Furman, Jaime; Shiverick, Kathleen T.

CS Department of Surgery, Division of Urology, College of Medicine, University of Florida, Gainesville, FL, USA

SO Prostate (New York, NY, United States) (2002), 52(3), 201-212 CODEN: PRSTDS; ISSN: 0270-4137

PB Wiley-Liss, Inc.

DT Journal

LA English

AB BACKGROUND. Isoflavones inhibit the growth of some types of tumor cells, including prostate adenocarcinoma. This study used LNCaP cells and xenografts to investigate the mechanisms of the antiproliferative effects of biochanin A, a major isoflavone present in red clover but not soy-derived products. METHODS. LNCaP cells were exposed to varying doses of biochanin A to evaluate viability, DNA synthesis, and DNA fragmentation (TUNEL) anal. Regulation of gene expression was detd. by using Western immunoblotting and cDNA microarrays. Anti-tumorigenic effects were evaluated by using athymic mice with LNCaP flank tumors. RESULTS. Biochanin A induced a dose-dependent inhibition of proliferation and [3H]thymidine incorporation that \*\*\*correlated\*\*\* with increased DNA fragmentation, indicative of apoptosis. Western blot analyses of cell cycle regulatory proteins revealed that biochanin A significantly decreased expression of cyclin B and p21, whereas flow cytometry showed that cells were accumulating in the G0/G1 phase. CDNA microarray analyses identified 29 down-regulated genes with six reduced below \*\*\*assay\*\*\* detection limits. Eleven genes were up-regulated, including 9 that were undetectable in controls. In mice with LNCaP xenografts, biochanin A significantly reduced tumor size and incidence. CONCLUSION. These results indicate that biochanin A inhibits prostate cancer cell growth through induction of cell cycle arrest and apoptosis. Biochanin A-regulated genes suggest multiple pathways of action. Biochanin A inhibits the incidence and growth of LNCaP xenograft tumors in athymic mice.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 131 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:640230 CAPLUS

DN 137:308455

TI Identify metastasis-associated genes in hepatocellular carcinoma through clonality delineation for multinodular tumor  
AU Cheung, Siu Tim; Chen, Xin; Guan, Xin Yuan; Wong, San Yu; Tai, Lai Shan; Ng, Irene O. L.; So, Samuel; Fan, Sheung Tat  
CS Department of Surgery, Centre for the Study of Liver Disease, The University of Hong Kong Medical Centre, Queen Mary Hospital, Hong Kong, Peop. Rep. China

SO Cancer Research (2002), 62(16), 4711-4721 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB Disease recurrence and metastasis are frequently obsd. in many successfully treated localized cancers, including hepatocellular carcinoma in which intrahepatic and extrahepatic recurrence (metastasis) are frequently obsd. after curative resection. The present study aimed at identifying metastasis-assocd. genes through delineation of the clonality for multinodular liver cancer. The clonal relationship of 22 tumor foci from six patients was investigated by the genome-wide \*\*\*expression\*\*\* \*\*\*profile\*\*\* via cDNA microarray consisting of 23,000 genes. Tumor mol. properties including p53 protein overexpression and gene mutation, hepatitis B virus integration pattern, and genetic alteration examd. by comparative genomic hybridization were compared. Results indicated that \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*patterns\*\*\* could serve as the mol. fingerprint for clonality identification. Together with the mol. data from p53, hepatitis B virus integration and comparative genomic hybridization profiles, tumor nodules from five patients were confirmed with clonal relationship, and the \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of the primary nodules were compared with their corresponding intrahepatic metastatic nodules. A total of 90 clones were found to be \*\*\*correlated\*\*\* with intrahepatic metastasis by Student's t \*\*\*test\*\*\* ( $P < 0.05$ ). With ref. to the primary tumor, 63 clones (39 known genes and 24 express sequence tags) were down-regulated whereas 27 clones (14 known genes and 13 express sequence tags) were up-regulated in the metastatic nodules. These metastasis-assocd. genes may provide clues to reveal patients with increased risk of developing metastasis, and to identify novel therapeutic targets for the treatment of metastasis.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 132 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:591234 CAPLUS

DN 137:333324

TI Differential induction of transcription factors and expression of milk protein genes by prolactin and growth hormone in the mammary gland of rabbits

AU Malewski, T.; Gajewska, M.; Zebrowska, T.; Zwierzchowski, L.

CS Institute of Genetics and Animal Breeding, Polish Academy of Sciences, Wolka Kosowska, 05-552, Pol.

SO Growth Hormone & IGF Research (2002), 12(1), 41-53

CODEN: GHIRF9; ISSN: 1096-6374

PB Elsevier Science Ltd.

DT Journal

LA English

AB Previously we demonstrated that administration of lactogenic hormones- prolactin (PRL) and growth hormone (GH) - to pregnant rabbits differentially induces expression of casein and whey proteins in the mammary gland. Now we extend these observations to transcription factors (TFs) that are responsive for differential induction of milk protein genes. Anal. of \*\*\*correlation\*\*\* between the no. of putative TF binding sites in 5'-upstream sequences and the levels of induction of milk protein genes allowed preselection of the TFs involved. An electrophoretic mobility shift \*\*\*assay\*\*\* with nuclear proteins derived from rabbit mammary glands showed changes in the patterns of Stat5, MAF, NF1 and Oct1 DNA-protein binding during progression of pregnancy and transition to lactation.

Administration of lactogenic hormones - PRL or GH - to early-pregnant rabbits induced DNA-protein complexes similar to those formed by nuclear proteins from the mammary glands of lactating (Stat5, MAF, NF1) or late-pregnant (Oct1) animals. Induction of milk protein genes by PRL was several-fold greater than that by GH. However, PRL and GH similarly induced MAF DNA-protein complexes, thus suggesting that the amt. of MAF factor in the mammary gland can be limiting for expression of these genes. Our study for the first time provided the evidence that in the mammary gland both PRL and GH can induce DNA-binding activity of transcription factors other than Stats.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 133 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:579697 CAPLUS

DN 138:50695

TI Molecular profiling of angiogenesis markers

AU Shih, Shu-Ching; Robinson, Gregory S.; Perruzzi, Carole A.; Calvo, Alfonso; Desai, Kartiki; Green, Jeffery E.; Ali, Iqbal U.; Smith, Lois E. H.; Senger, Donald R.

CS Department of Ophthalmology, Children's Hospital, Harvard Medical School, Boston, MA, USA

SO American Journal of Pathology (2002), 161(1), 35-41

CODEN: AJPA44; ISSN: 0002-9440

PB American Society for Investigative Pathology

DT Journal

LA English

AB The goal of this study was to develop a sensitive, simple, and widely applicable **\*\*\*assay\*\*\*** to measure copy nos. of specific mRNAs using real-time quant. reverse transcriptase-polymerase chain reaction (RT-PCR), and identify a **\*\*\*profile\*\*\*** of **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** closely assocd. with angiogenesis. We measured a panel of nine potential angiogenesis markers from a mouse transgenic model of prostate adenocarcinoma (TRAMP) and a mouse skin model of vascular endothelial growth factor (VEGF)-driven angiogenesis. In both models, expression of VEGF **\*\*\*correlated\*\*\*** with expression of mRNAs encoding other angiogenic cytokines (angiopoietin-1 and angiopoietin-2), endothelial cell receptor tyrosine kinases (Flt-1, KDR, Tie-1), and endothelial cell adhesion molts. (VE-cadherin, PECAM-1). Relative to control, in dermis highly stimulated by VEGF, the Ang-2 mRNA transcript nos. increased 35-fold, PECAM-1 and VE-cadherin increased 10-fold, Tie-1 increased 8-fold, KDR and Flt-1 each increased 4-fold, and Ang-1 increased 2-fold. All transcript nos. were correspondingly reduced in skin with less VEGF expression, indicating a relationship of each of these seven markers with VEGF. Thus, this study identifies a highly efficient method for precise quantification of a panel of seven specific mRNAs that **\*\*\*correlate\*\*\*** with VEGF expression and VEGF-induced neovascularization, and it provides evidence that real-time quant. RT-PCR offers a highly sensitive strategy for monitoring angiogenesis.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 134 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:549620 CAPLUS

DN 137:292541

TI Combined use of oligonucleotide and tissue microarrays identifies cancer/ **\*\*\*testis\*\*\*** antigens as biomarkers in lung carcinoma

AU Sugita, Michio; Geraci, Mark; Gao, Bifeng; Powell, Roger L.; Hirsch, Fred R.; Johnson, Gary; Lapadat, Razvan; Gabrielson, Edward; Bremnes, Roy; Bunn, Paul A.; Franklin, Wilbur A.

CS Department of Pathology, University of Colorado Health Sciences Center, Denver, CO, 80262, USA

SO Cancer Research (2002), 62(14), 3971-3979 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB High d. oligonucleotide microarrays (OMAs) have been used recently to **\*\*\*profile\*\*\*** **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** in lung carcinoma tissue homogenates. The length of the lists of potentially interesting genes generated by these studies is daunting, and biol. and clin. relevance of these lists remains to be validated. Moreover, specific identification of individual biomarkers that might be used for early detection and surveillance has not been the objective of these early studies. We have developed a schema for combining the data derived from the OMA anal. of a few lung cancer cell lines with immunohistochem. **\*\*\*testing\*\*\*** of tissue microarrays to rapidly identify biomarkers of potential clin. relevance. Initially, we **\*\*\*profiled\*\*\*** **\*\*\*gene\*\*\*** **\*\*\*expression\*\*\*** in lung tumor cell lines using the Affymetrix HG-U95Av2 OMA. RNA from 2 non-small cell lung cancer (NSCLC) cell lines (A549 and H647) and 2 small cell lung cancer (SCLC) cell lines (SHP-77 and UMC-19) were **\*\*\*tested\*\*\***. Cells from 1 histol. and cytogenetically normal bronchial epithelial primary culture from a volunteer who had never smoked and 10 samples of histol. unremarkable lung tissue from resection specimens served as normalization controls. Array results were analyzed with Gene Spring software. Results were confirmed by reverse transcription-PCR in an expanded no. of cell lines. We then validated the cell line data by immunohistochem. **\*\*\*testing\*\*\*** for protein using a tissue microarray contg. 187 NSCLC clin. samples. Of the 20 most highly expressed genes in the tumor lines, 6 were members of the cancer/ **\*\*\*testis\*\*\*** antigen (CTAG) gene group including 5 MAGE-A subfamily members and NY-ESO-1. SCLC lines strongly expressed all of the MAGE-A genes as well as NY-ESO-1, whereas NSCLC lines expressed a subset of MAGE-A genes at a lower level of intensity and failed to express NY-ESO-1. Reverse transcription-PCR of an extended series of 25 lung cancer cell lines including 13 SCLC, 9 NSCLC, and 3 mesothelioma lines indicated that MAGE-A10 and NY-ESO-1 were expressed only by SCLC, and that MAGE-A1, 3, 6, 12, and 4b were expressed by both SCLC and NSCLC. By immunohistochem. using the monoclonal antibody 6C1 that recognizes several MAGE-A gene subfamily members, 44% of NSCLC clearly expressed MAGE-A proteins in cytoplasm and/or nucleus. Expression of MAGE-A genes did not **\*\*\*correlate\*\*\*** with survival but did **\*\*\*correlate\*\*\*** with histol. classification with squamous carcinomas more frequently MAGE-A pos. than other NSCLC types (P < 0.00002). We conclude that expression of CTAG gene products, whereas apparently not of prognostic importance, may be useful for early detection and surveillance because of a high level of specificity for central airway squamous and small cell carcinomas.

RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 135 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:548465 CAPLUS

DN 137:74491

TI Novel nucleic acids and their encoded proteins useful for identification, assessment, prevention, and therapy of human ovarian cancer

IN Lee, John; Lillie, James

PA Millennium Predictive Medicine, Inc., USA

SO PCT Int. Appl., 106 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001070979	A2	20010927	WO 2001-US9126	
	20010321	WO	2001070979	A3	20020704
C2	20020801	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
	2003165831	A1	20030904	US 2001-814353	
	20010321				
PRAI	US 2000-191031P	P	20000321	US 2000-207124P	
P	20000525	US	2000-211940P	P	20000615
	2000-216820P	P	20000707	US 2000-220661P	P
	20000725	US	2000-257672P	P	20001221

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers. Subtracted cDNA libraries are generated using a PCR-based method that allows the isolation of clones expressed at higher levels in one population of mRNA compared to another population. The cDNA libraries were constructed from normal ovarian epithelial cell cultures, ascites short cultured samples from ovarian cancer patients, and serous late stage tumor samples. Nearly 6400 cDNAs were isolated and sequenced that are differentially expressed in ovarian cancer. Re-interpretation of these sequences and removal of vector sequences yielded an addnl., 15,639 partial cDNA sequences. Thus, a variety of novel markers are provided, wherein changes in the levels of expression of one or more of the markers is \*\*\*correlated\*\*\* with the presence of ovarian cancer.

L9 ANSWER 136 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:547946 CAPLUS

DN 138:265552

TI Expression of c-Myc and other apoptosis-related genes in Swiss Webster mouse fetuses after maternal exposure to all trans-retinoic acid

AU Sarkar, Suparna A.; Sharma, Raghubir P.

CS College of Veterinary Medicine, Department of Physiology and Pharmacology, The University of Georgia, Athens, GA, 30602-7389, USA

SO Reproductive Toxicology (2002), 16(3), 245-252 CODEN: REPTED; ISSN: 0890-6238

PB Elsevier Science Inc.

DT Journal

LA English

AB The Myc family of genes regulates proliferation, differentiation, and apoptosis. Temporal expression of Myc family genes and several pro-apoptotic genes were investigated

during Swiss Webster mice organogenesis after maternal treatment with an oral dose of 100 mg/kg trans-retinoic acid (RA) or vehicle on day 10 post-coitum. Reverse transcriptase-polymerase chain reaction and RNase protection \*\*\*assay\*\*\* revealed decreased c-myc expression at 48 h followed by an increase at 72 h in fetuses from RA-treated dams. Increased c-Myc protein was detected at 72 h in the RA-treated group. In utero RA-treatment resulted in decreased expression of max, mad, caspases, bax, and bad genes at 48 h. Terminal uridinetriphosphate nick end-labeling (TUNEL) anal. revealed increased apoptosis at 24-48 h, followed by decreased apoptosis 72 h after in utero RA-exposure, which \*\*\*correlated\*\*\* with the decreased expression of pro-apoptotic genes noted at 48 h. Further investigations are needed to understand the role of Myc family genes during RA-mediated teratogenesis.

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 137 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:524877 CAPLUS

DN 137:308309

TI \*\*\*Expression\*\*\* \*\*\*profile\*\*\* of genes in non-small cell lung carcinomas from long-term surviving patients

AU Volm, Manfred; Koomagi, Reet; Mattern, Juergen; Efferth, Thomas

CS German Cancer Research Center, Heidelberg, 69120, Germany

SO Clinical Cancer Research (2002), 8(6), 1843-1848 CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB Non-small cell lung cancer (NSCLC) is usually assocd. with a poor prognosis. Some patients survive their disease, and the underlying mol. mechanisms are still poorly understood. The purpose of this investigation was to evaluate \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of proteins detg. the survival of NSCLC patients for 5 yr. The expression of 21 gene products was evaluated immunohistochem. in paraffin-embedded primary NSCLCs from 216 patients. The data were \*\*\*correlated\*\*\* with the survival times of the patients (survival of more or less than 5 yr) by means of .chi.2 \*\*\*test\*\*\* and hierarchical cluster anal. The relationships of patients' survival and 21 parameters were detd. including oncogene and tumor suppressor products and proliferative, apoptotic, and angiogenic factors. FOS, P53, RAS, ERBB1, JUN, PCNA, cyclin A, FAS/CD95, and HIF-1.beta. revealed a \*\*\*correlation\*\*\* to survival. In a second step, these nine parameters were further analyzed by hierarchical cluster analyses of all patients, of stage III patients, and of patients with squamous cell lung carcinomas. The authors identified clusters with significantly more long-term survivors. The expression of FOS, JUN, ERBB1, and cyclin A or PCNA were decreased in carcinomas of patients with long-term survival. The \*\*\*expression\*\*\* \*\*\*profile\*\*\* of these factors predicts a significantly better long-term outcome of NSCLC patients. This may have implications for the development of individualized therapy options in the future.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 138 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:519282 CAPLUS

DN 137:307883

TI Deciphering peripheral nerve myelination by using Schwann cell \*\*\*expression\*\*\* \*\*\*profiling\*\*\*

AU Nagarajan, Rakesh; Le, Nam; Mahoney, Heather; Araki, Toshiyuki; Milbrandt, Jeffrey

CS Departments of Pathology and Internal Medicine, Washington University School of Medicine, St. Louis, MO, 63110, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2002), 99(13), 8998-9003 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Although mutations in multiple genes are assocd. with inherited demyelinating neuropathies, the mol. components and pathways crucial for myelination remain largely unknown. To approach this question, we performed genome-wide expression anal. in several paradigms where the status of peripheral nerve myelination is dynamically changing. Anchor gene \*\*\*correlation\*\*\* anal., a form of microarray anal. that integrates functional information, using \*\*\*correlation\*\*\* - based clustering, with a statistically rigorous \*\*\*test\*\*\*, the Westfall and Young step-down algorithm, was applied to this data set. Biol. pathways active in myelination, genes encoding proteins involved in myelin synthesis, and genes whose mutation results in myelination defects were identified. Many known genes and previously uncharacterized ESTs not heretofore assocd. with myelination were also identified. One of these ESTs, MASR (myelin-assocd. SUR4 protein), encodes a member of the SUR4 family of fatty acid desaturases, enzymes involved in elongation of very long chain fatty acids. Its specific localization in myelinating Schwann cells indicates a crucial role for MASR in normal myelin lipid synthesis.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 139 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:499636 CAPLUS

DN 137:42671

TI Novel nucleic acids and their encoded proteins useful for identification, assessment, prevention, and therapy of human ovarian cancer

IN Lee, John; Lillie, James

PA Millennium Predictive Medicine, Inc., USA

SO PCT Int. Appl., 106 pp. CODEN: PIXXD2

DT Patent

LA English PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001070979 A2 20010927 WO 2001-US9126 20010321 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: AB, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR  
PRAI US 2000-2000/PV19103U 20000321 US 2000-2000/PV20712U 20000525 US 2000-2000/PV21194U 20000615 US 2000-2000/PV21682U 20000707 US 2000-2000/PV22066U 20000725 US 2000-2000/PV257672 20001221

AB The invention relates to compns., kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers. Subtracted cDNA libraries are generated using a PCR-based method that allows the isolation of clones expressed at higher levels in one population of mRNA compared to another population. The cDNA libraries were constructed from normal ovarian epithelial cell cultures, ascites short cultured samples from ovarian cancer patients, and serous late stage tumor samples. Nearly 6400 cDNAs were isolated and sequenced that are differentially expressed in ovarian cancer. Re-interpretation of these sequences and removal of vector sequences yielded an addnl., 15,639 partial cDNA sequences. Thus, a variety of novel markers are provided, wherein changes in the levels of expression of one or more of the markers is \*\*\*correlated\*\*\* with the presence of ovarian cancer.

L9 ANSWER 140 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:448975 CAPLUS

DN 137:227131

TI RNA amplification results in reproducible microarray data with slight ratio bias

AU Puskas, Laszlo G.; Zvara, Agnes; Hackler, Laszlo, Jr.; Van Hummelen, Paul

CS Hungarian Academy of Sciences, Szeged, Hung.

SO BioTechniques (2002), 32(6), 1330-1334, 1336, 1338, 1340 CODEN: BTNQDO; ISSN: 0736-6205

PB Eaton Publishing Co.

DT Journal

LA English

AB Microarray expression anal. demands large amts. of RNA that are often not available. RNA amplification techniques have been developed to overcome this problem, but limited data are available regarding the reproducibility and maintenance of original transcript ratios. We optimized and validated two amplification techniques: a modified in vitro transcription for the linear amplification of 3 .mu.g total RNA and a SMART PCR-based technique for the exponential amplification of 50 ng total RNA. To det. bias between transcript ratios, we compared the \*\*\*expression\*\*\* \*\*\*profiles\*\*\* in mouse \*\*\*testis\*\*\* vs. spleen between the two amplification methods and a std. labeling protocol, using microarrays contg. 4596 cDNAs spotted in duplicate. With each method, replicate hybridizations were highly reproducible. However, when comparing the amplification methods to std. labeling, \*\*\*correlation\*\*\* coeffs. were lower. Twelve genes that exhibited inconsistent or contradictory expression ratios among the three methods were verified by quant. RT-PCR. The amplification methods showed slightly more discrepancies in the expression ratios when compared to quant. RT-PCR results but were more sensitive in terms of detecting expressed genes. In conclusion, although amplification methods introduce slight changes in the transcript ratios compared to std. labeling, they are highly reproducible. For small sample size, in vitro transcription is the preferred method, but one should never combine different labeling strategies within a single study.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 141 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:432008 CAPLUS

DN 137:349732

TI Spermatogonia-dependent expression of \*\*\*testicular\*\*\* genes in mice



AU Tanaka, Kiyoko; Tamura, Hiroshi; Tanaka, Hiromitsu; Katoh, Masaki; Futamata, Yoshiki; Seki, Naohiko; Nishimune, Yoshitake; Hara, Takahiko

CS Department of Tumor Biochemistry, The Tokyo Metropolitan Institute of Medical Science, Tokyo Metropolitan Organization for Medical Research, Bunkyo-ku, Tokyo, 113-8613, Japan

SO Developmental Biology (Orlando, FL, United States) (2002), 246(2), 466-479 CODEN: DEBIAO; ISSN: 0012-1606

PB Elsevier Science

DT Journal

LA English

AB Spermatogenesis is initiated by the interaction of germ cells and somatic cells in seminiferous tubules. We used cDNA microarrays and representational difference anal. to identify genes that are expressed in the \*\*\*testis\*\*\* of the jsd/jsd mutant mouse, which contains only type A spermatogonial germ cells and Sertoli cells, but not in the \*\*\*testis\*\*\* of the W/Wv mutant mouse, where Sertoli cells but few germ cells are present. We isolated 20 known genes and 4 novel genes, including 2 genes encoding lipocalin family members (prostaglandin D synthetase and 24p3) and 2 tumor suppressors (protein tyrosine phosphatase TD14 and Sui1). All 24 of these jsd/jsd-derived genes were highly expressed in the cryptorchid \*\*\*testis\*\*\* as well as in the jsd/jsd \*\*\*testis\*\*\*. This indicates that their selective expression is not directly caused by the as-yet-uncharacterized jsd gene product, but is rather \*\*\*correlated\*\*\* to the cessation of spermatogonial differentiation. In situ hybridization anal. and flow cytometric sorting followed by reverse transcriptase-PCR revealed that these genes are expressed in both the spermatogonial germ cells and the somatic cells in the developing gonads and adult \*\*\*testes\*\*\*. As the mRNAs of these jsd/jsd-derived genes were barely detectable in the W/Wv \*\*\*testis\*\*\*, we propose that early spermatogonial germ cells regulate the expression of a group of \*\*\*testicular\*\*\* genes.

RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 142 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:431975 CAPLUS

DN 137:29302

TI Aroclor 1254 Modulates Gene Expression of Nuclear Transcription Factors: Implications for Albumin Gene Transcription and Protein Synthesis in Rat Hepatocyte Cultures

AU Borlak, Juergen; Dangers, Marc; Thum, Thomas

CS Fraunhofer Institute of Toxicology and Aerosol Research, Center for Drug Research and Medical Biotechnology, Hannover, D-30659, Germany

SO Toxicology and Applied Pharmacology (2002), 181(2), 79-88 CODEN: TXAPA9; ISSN: 0041-008X

PB Elsevier Science

DT Journal

LA English

AB Human exposure to polychlorinated biphenyls (PCBs) may lead to increased albumin serum levels, but little is known about the underlying events. Certain PCBs are also ligands for the aryl hydrocarbon receptor (Ahr) and this receptor regulates transcriptional activation of many different genes, including CYP1A1. We \*\*\*tested\*\*\* our hypothesis that expression of certain nuclear transcription factors is altered upon treatment of rat hepatocyte cultures with Aroclor 1254 and we studied the gene expression of albumin and liver-enriched transcription factors simultaneously. We \*\*\*correlate\*\*\* albumin gene expression with protein synthesis and we used CYP1A1 gene

expression and enzyme activity as a surrogate endpoint for aryl hydrocarbon receptor activation. We found mRNA transcripts of CCAAT/enhancer binding protein .alpha. and .gamma., hepatic nuclear factor 1, and hepatic nuclear factor 4 to be increased up to 62-fold, whereas albumin gene expression and secretion was increased 3-fold. Noticeably, expression of c-fos, c-jun (AP-1), HNF-6, CCAAT/enhancer binding protein .beta. and .delta., tissue-specific enhancer-1, Ah-receptor, and albumin D-site-binding protein was unchanged. We show coordinate albumin gene expression and protein secretion in primary rat hepatocyte cultures and propose a relationship between induction of certain liver-enriched transcription factors and of the albumin gene via an Ahr-mediated mechanism.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 143 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:429112 CAPLUS

DN 137:16481

TI Detecting aneuploidy by \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* using DNA microarray and its diagnostic application

IN Marton, Matthew J.; Hughes, Timothy R.

PA Rosetta Inpharmatics, Inc., USA

SO PCT Int. Appl., 137 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	---	-----	-----
PI	WO 2002044411	A1	20020606	WO 2000-US35352	
	20001222	W: CA, JP			
PRAI	US 2000-250597P	P	20001201		

AB The present invention relates to methods for detecting aneuploidy or, in particular, detg. the likelihood that aneuploidy is present in a cell type or organism. In particular, the invention relates to the use of profiles for detecting aneuploidy or for detg. the likelihood of the presence of aneuploidy in a cell type or organism that is assocd. with a disease, or with a predisposition toward a certain disease. The present invention also relates to methods of correcting a profile for the presence of aneuploidy. The present further invention relates to a computer system, a computer program product and kits for detecting aneuploidy or detg. the likelihood that aneuploidy is present in a cell type or organism. The method is demonstrated by the detection of aneuploidy in yeast knockout strains as well as publicly available expression data obtained using SAGE and using microarrays. A large no. of the mutants profiled exhibited chromosome-wide expression biases, leading to spurious \*\*\*correlations\*\*\* among profiles. The invention has implications for interpreting whole-genome expression data, particularly from cells known to suffer genomic instability, such as malignant or immortalized cells.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 144 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:420684 CAPLUS

DN 137:16670

TI Prediction of compound signature using high density \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\*

AU Hamadeh, Hisham K.; Bushel, Pierre R.; Jayadev, Supriya; DiSorbo, Olimpia; Bennett, Lee; Li, Leping; Tennant, Raymond; Stoll, Raymond; Barrett, J. Carl; Paules, Richard S.; Blanchard, Kerry; Afshari, Cynthia A.

CS National Institute of Environmental Health Sciences, Research Triangle Park, NC, 27709, USA

SO Toxicological Sciences (2002), 67(2), 232-240 CODEN: TOSCF2; ISSN: 1096-6080

PB Oxford University Press

DT Journal

LA English

AB DNA microarrays, used to measure the gene expression of thousands of genes simultaneously, hold promise for future application in efficient screening of therapeutic drugs. This will be aided by the development and population of a database with \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\*

corresponding to biol. responses to exposures to known compds. whose toxicol. and pathol. endpoints are well characterized. Such databases could then be interrogated, using profiles corresponding to biol. responses to drugs after developmental or environmental exposures. A pos. \*\*\*correlation\*\*\* with an archived profile could lead to some knowledge regarding the potential effects of the \*\*\*tested\*\*\* compd. or exposure. We have previously shown that cDNA microarrays can be used to generate chem.-specific \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* that can be distinguished across and within compd. classes, using clustering, simple \*\*\*correlation\*\*\*, or principal component analyses. In this report, we \*\*\*test\*\*\* the hypothesis that knowledge can be gained regarding the nature of blinded samples, using an initial training set comprised of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* derived from rat liver exposed to dofibrate, Wyeth 14,643, gemfibrozil, or phenobarbital for 24 h or 2 wk of exposure. Highly discriminant genes were derived from our database training set using approaches including linear discriminant anal. (LDA) and genetic algorithm/K-nearest neighbors (GA/KNN). Using these genes in the anal. of coded liver RNA samples derived from 24-h, 3-day, or 2-wk exposures to phenytoin, diethylhexylphthalate, or hexobarbital led to successful prediction of whether these samples were derived from livers of rats exposed to enzyme inducers or to peroxisome proliferators. This validates our initial hypothesis and lends credibility to the concept that the further development of a gene expression database for chem. effects will greatly enhance the hazard identification processes.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 145 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:414958 CAPLUS

DN 137:150791

TI Computational identification of transcription factor binding sites via a transcription-factor-centric clustering (TFCC) algorithm  
AU Zhu, Zhou; Pilpel, Yitzhak; Church, George M.

CS Department of Genetics and Lippar Center for Computing and Genetics, Harvard Medical School, Boston, MA, 02115, USA

SO Journal of Molecular Biology (2002), 318(1), 71-81 CODEN: JMOBAK; ISSN: 0022-2836

PB Elsevier Science Ltd.

DT Journal

LA English

AB While microarray-based \*\*\*expression\*\*\* \*\*\*profiling\*\*\* has facilitated the use of computational methods to find potential cis-regulatory promoter elements, few current in silico approaches explicitly link regulatory motifs with

the transcription factors that bind them. We have thus developed a TF-centric clustering (TFCC) algorithm that may provide such missing information through incorporation of biol. knowledge about TFs. TFCC is a semi-supervised clustering algorithm which relies on the assumption that the \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of some TFs may be related to those of the genes under their control. We examd. this premise and found the vicinities of TFs in expression space are often enriched with the genes they regulate. So, instead of clustering genes based on the mutual similarity of their \*\*\*expression\*\*\* \*\*\*profiles\*\*\* to each other, we used TFs as seeds to group together genes whose expression patterns \*\*\*correlate\*\*\* with that of a particular TF. Then a Gibbs sampling algorithm was applied to search for shared cis-regulatory elements in promoters of clustered genes. Our working hypothesis was that if a TF-centric cluster indeed contains many targets of the seeding TF, at least one of the discovered motifs would be the site bound by the very same TF. We \*\*\*tested\*\*\* the TFCC approach on eight cell cycle and sporulation regulating TFs whose binding sites have been previously characterized in Saccharomyces cerevisiae, and correctly identified binding site motifs for half of them. In addn., we also made de novo predictions for some unknown TF binding sites.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 146 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:339284 CAPLUS

DN 138:33258

TI Activation of the nuclear transcription factor .kappa.B (NF.kappa.B) and differential gene expression in U87 glioma cells after exposure to the cytoprotector amifostine

AU Kataoka, Yasushi; Murley, Jeffrey S.; Khodarev, Nikolai N.; Weichselbaum, Ralph R.; Grdina, David J.

CS Department of Radiation and Cellular Oncology, University of Chicago, Chicago, IL, USA

SO International Journal of Radiation Oncology, Biology, Physics (2002), 53(1), 180-189 CODEN: IOBPD3; ISSN: 0360-3016

PB Elsevier Science Inc.

DT Journal

LA English

AB Purpose: Amifostine has been approved as a therapy to decrease the incidence of moderate-to-severe xerostomia in patients undergoing postoperative radiation treatment for head-and-neck cancer. As a reducing agent capable of participating in intracellular reductive/oxidative processes, it has the potential to affect redox-sensitive transcription factors and gene expression. Amifostine's active free thiol WR-1065 was investigated to det. its effect on nuclear transcription factor .kappa.B (NF.kappa.B) activation and subsequent gene expression in U87 glioma cells. Methods and Materials: The human glioma cell line U87 was grown to confluency and then exposed to WR-1065 at a concn. of 40 .mu.M for times ranging from 30 min to 24 h. Changes in cell cycle were monitored by flow cytometry. The effect of WR-1065 on NF.kappa.B activation was detd. by a gel shift \*\*\*assay\*\*\*. Changes in gene expression as a function of time of exposure to WR-1065 were detd. by Northern blot and the Atlas Human cDNA Expression Array (Clontech, Palo Alto, CA). Changes in gene expression using the Atlas Array were verified by reverse transcriptase-polymerase chain reaction (RT-PCR) with gene-specific primers. Results: Exposure of U87 cells to 40 .mu.M WR-1065 resulted in a marked activation of NF.kappa.B between 30 min and 1 h after treatment. Expression of MnSOD,

an NF.kappa.B-responsive gene, was enhanced by over 2-fold after 16 h of treatment and remained elevated at 24 h. During this period of time, no changes in cell cycle distribution were obsd. To assess changes in the expression levels of NF.kappa.B-responsive genes as a function of WR-1065 exposure, cDNA arrays contg. 49 genes identified as having DNA-binding motifs for NF.kappa.B were used. Only five genes were found to be significantly affected at 1, 4, and/or 16 h of treatment. GST-3 and c-myc were repressed up to 2- and 4-fold, resp. The expression levels of IL-2Ra, RANTES, and c-myc, in contrast, were enhanced up to 14-, 3-, and 2-fold, resp. The remaining genes having NF.kappa.B-responsive elements in their promoter regions were either not expressed (20 genes) or were not affected (24 genes) by exposure to WR-1065. Conclusions: The redox-sensitive transcription factor NF.kappa.B can be activated in U87 glioma cells by the active thiol form of the cytoprotector amifostine. Activation of NF.kappa.B by the antioxidant WR-1065 is accompanied by a reduced expression of the oncogene c-myc and an enhanced expression of the antioxidant gene MnSOD, a gene whose expression in tumor cells is relatively low, but when overexpressed has been \*\*\*correlated\*\*\* with a suppression of the malignant phenotype. Activation of NF.kappa.B by WR-1065, however, results in selective rather than global changes in the expression of genes contg. NF.kappa.B-responsive elements. RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 147 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:324182 CAPLUS

DN 137:214524

TI Osteopontin identified as lead marker of colon cancer progression, using pooled sample \*\*\*expression\*\*\*  
\*\*\*profiling\*\*\*

AU Agrawal, Deepak; Chen, Tingan; Irby, Rosalyn; Quackenbush, John; Chambers, Ann F.; Szabo, Marianna; Cantor, Alan; Coppola, Domenico; Yeatman, Timothy J.

CS Department of Cell Biology, H. Lee Moffitt Cancer Center, Interdisciplinary Oncology, University of South Florida, Tampa, FL, 33612, USA

SO Journal of the National Cancer Institute (2002), 94(7), 513-521 CODEN: JNCIEQ; ISSN: 0027-8874

PB Oxford University Press

DT Journal

LA English

AB New tumor markers and markers of tumor progression are needed for improved staging and for better assessment of treatment of many cancers. \*\*\*Gene\*\*\* \*\*\*expression\*\*\*  
\*\*\*profiling\*\*\* techniques offer the opportunity to discover such markers. We investigated the feasibility of sample pooling strategy in combination with a novel anal. algorithm to identify markers. Total RNA from human colon tumors (n = 60) of multiple stages (adenomas; cancers with modified Astler Collier stages B, C, and D; and liver metastases) were pooled within stages and compared with pooled normal mucosal specimens (n = 10) by oligonucleotide expression arrays. Genes that showed consistent increases or decreases in their expression through tumor progression were identified. Northern blot anal. was used to validate the findings. All statistical \*\*\*tests\*\*\* were 2-sided. More than 300 candidate tumor markers and more than 100 markers of tumor progression were identified. Northern anal. of 11 candidate tumor markers confirmed the gene expression changes. The gene for the secreted integrin binding protein osteopontin was most consistently differentially expressed in conjunction with tumor progression. Its potential as a

progression marker was validated (Spearman's .rho. = 0.903; P<.001) with northern blot anal. using RNA from an independent set of 10 normal and 43 tumor samples representing all stages. Moreover, a statistically significant \*\*\*correlation\*\*\* between osteopontin protein expression and advancing tumor stage was identified with the use of 303 addnl. specimens (human cancer = 185, adenomas = 67, and normal mucosal specimens = 51) (Spearman's .rho. = 0.667; P<.001). Sample pooling can be a powerful, cost-effective, and rapid means of identifying the most common changes in a \*\*\*gene\*\*\* \*\*\*expression\*\*\*  
\*\*\*profile\*\*\*. We identified osteopontin as a clin. useful marker of tumor progression by \*\*\*gene\*\*\*  
\*\*\*expression\*\*\* \*\*\*profiling\*\*\* on pooled samples. RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 148 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:284284 CAPLUS

DN 137:305437

TI Identification and characterisation of known and novel transcripts expressed during the final stages of human oocyte maturation

AU Goto, Tetsuya; Jones, Gayle M.; Lolatgis, Nick; Pera, Martin F.; Trounson, Alan O.; Monk, Marilyn

CS Centre for Early Human Development, Monash Medical Centre, Institute of Reproduction and Development, Clayton, 3168, Australia

SO Molecular Reproduction and Development (2002), 62(1), 13-28 CODEN: MREDEE; ISSN: 1040-452X

PB Wiley-Liss, Inc.

DT Journal

LA English

AB The final stages of oocyte maturation, from the germinal vesicle (GV) stage to metaphase II (MII) oocytes, are characterized by a series of dynamic events. These include germinal vesicle break down (GVBD), resumption of meiosis, and nuclear and cytoplasmic maturation to produce MII oocytes ready for fertilization. To investigate the specific genes transcribed during these stages of oogenesis, we have prepd. and analyzed amplified cDNA representing the transcribed genes in a series of GV and MII oocytes. Differential display anal. disclosed that the overall \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* between different samples of GV oocytes are very similar, regardless of their source, while those between the MII oocytes are markedly variable. A comparison of \*\*\*expression\*\*\*  
\*\*\*profiles\*\*\* in oocytes and somatic (cumulus) cells identified several known genes preferentially-expressed in oocytes (e.g., a zona pellucida gene), as well as five novel sequences. Two of the five novel sequences are homologous to retrotransposon sequences, long terminal repeat (LTR) and long interspersed nuclear element (LINE) 1, and two other sequences show partial homol. to known ESTs and genomic sequences. The remaining sequence, which is identical to shorter ESTs isolated from germ cell tumor cDNA libraries, was extended towards its 5' end by PCR, using the original cDNA prepn. from which it was isolated as a template. Expression of the resultant 1.1-kb transcript is restricted to the \*\*\*testis\*\*\* and ovary, and its expression \*\*\*correlates\*\*\* with cell pluripotency in that it is expressed in embryonal carcinoma cells, but not in their differentiated deriv. cells.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 149 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:250061 CAPLUS  
DN 136:226221  
TI cDNA microarray technology as a laboratory examination methods: A \*\*\*gene\*\*\* \*\*\*expression\*\*\*  
\*\*\*profiling\*\*\* \*\*\*test\*\*\* for analysis of drug resistance in tumor cells  
AU Miyachi, Hayato; Kobayashi, Hiroyuki; Asai, Satomi; Shinbata, Tomoya; Arami, Shinichiro; Mitsuse, Shizuo  
CS Dep. Lab. Med., Tokai Univ. Sch. Med., Isehara, 259-1193, Japan  
SO Rinsho Byori (2002), 50(2), 161-168 CODEN: RBYOAI; ISSN: 0047-1860  
PB Nippon Rinsho Kensa Igakkai  
DT Journal; General Review  
LA Japanese  
AB A review. CDNA microarray technol. permits the simultaneous measurement of the expressions of thousands of genes. The technol. is now an indispensable research tool in mol. biol., and the challenge is its development and usage as clin. diagnostic tools. CDNA microarray can be used to identify \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* in tumor cells which \*\*\*correlate\*\*\* strongly with the treatment responsiveness such as drug resistance and clin. outcome of the disease despite similar phenotypes. For the introduction of cDNA microarray into lab. examn., many issues need to be resolved. Design of a diagnostic array must be developed with defined sequences based on interpretation of huge quantities of data from exptl. arrays to predict treatment responsiveness. \*\*\*Assay\*\*\* quality must be improved in terms of detection sensitivity, reproducibility, and linear dynamic range of RNA quantitation. Generally available instruments, which are much less expensive and more practical, need to be developed. Along with the improvement of the \*\*\*assay\*\*\* as a lab. examn. method, cDNA microarray will facilitate the integration of diagnosis and therapeutics, and the introduction of individual medicines.

L9 ANSWER 150 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:226441 CAPLUS  
DN 137:104340  
TI Inference from clustering with application to gene-expression microarrays  
AU Dougherty, Edward R.; Barrera, Junior; Brun, Marcel; Kim, Seungchan; Cesar, Roberto M.; Chen, Yidong; Bittner, Michael; Trent, Jeffrey M.  
CS Department of Electrical Engineering, Texas A and M University, College Station, TX, 77840, USA  
SO Journal of Computational Biology (2002), 9(1), 105-126 CODEN: JCOBEM; ISSN: 1066-5277  
PB Mary Ann Liebert, Inc.  
DT Journal  
LA English  
AB There are many algorithms to cluster sample data points based on nearness or a similarity measure. Often the implication is that points in different clusters come from different underlying classes, whereas those in the same cluster come from the same class. Stochastically, the underlying classes represent different random processes. The inference is that clusters represent a partition of the sample points according to which process they belong. This paper discusses a model-based clustering toolbox that evaluates cluster accuracy. Each random process is modeled as its mean plus independent noise, sample points are generated, the points are clustered, and the clustering error is the no. of

points clustered incorrectly according to the generating random processes. Various clustering algorithms are evaluated based on process variance and the key issue of the rate at which algorithmic performance improves with increasing nos. of exptl. replications. The model means can be selected by hand to \*\*\*test\*\*\* the separability of expected types of biol. expression patterns. Alternatively, the model can be seeded by real data to \*\*\*test\*\*\* the expected precision of that output or the extent of improvement in precision that replication could provide. In the latter case, a clustering algorithm is used to form clusters, and the model is seeded with the means and variances of these clusters. Other algorithms are then \*\*\*tested\*\*\* relative to the seeding algorithm. Results are averaged over various seeds. Output includes error tables and graphs, confusion matrixes, principal-component plots, and validation measures. Five algorithms are studied in detail: K-means, fuzzy C-means, self-organizing maps, hierarchical Euclidean-distance-based and \*\*\*correlation\*\*\* -based clustering. The toolbox is applied to gene-expression clustering based on cDNA microarrays using real data. \*\*\*Expression\*\*\* \*\*\*profile\*\*\* graphics are generated and error anal. is displayed within the context of these profile graphics. A large amt. of generated output is available over the web.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 151 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:213429 CAPLUS  
DN 137:211484  
TI Inference of a genetic network by a combined approach of cluster analysis and graphical Gaussian modeling  
AU Toh, Hiroyuki; Horimoto, Katsuhisa  
CS Department of Bioinformatics, Biomolecular Engineering Research Institute, Osaka, 565-0874, Japan  
SO Bioinformatics (2002), 18(2), 287-297 CODEN: BOINFP; ISSN: 1367-4803  
PB Oxford University Press  
DT Journal  
LA English  
AB Motivation: Recent advances in DNA microarray technologies have made it possible to measure the expression levels of thousands of genes simultaneously under different conditions. The data obtained by microarray analyses are called \*\*\*expression\*\*\* \*\*\*profile\*\*\* data. One type of important information underlying the \*\*\*expression\*\*\* \*\*\*profile\*\*\* data is the 'genetic network,' i.e., the regulatory network among genes. Graphical Gaussian Modeling (GGM) is a widely utilized method to infer or \*\*\*test\*\*\* relationships among a plural of variables. Results: In this study, we developed a method combining the cluster anal. with GGM for the inference of the genetic network from the \*\*\*expression\*\*\* \*\*\*profile\*\*\* data. The \*\*\*expression\*\*\* \*\*\*profile\*\*\* data of 2467 *Saccharomyces cerevisiae* genes measured under 79 different conditions were used for this study. At first, the 2467 genes were classified into 34 clusters by a cluster anal., as a preprocessing for GGM. Then, the expression levels of the genes in each cluster were averaged for each condition. The averaged \*\*\*expression\*\*\* \*\*\*profile\*\*\* data of 34 clusters were subjected to GGM, and a partial \*\*\*correlation\*\*\* coeff. matrix was obtained as a model of the genetic network of *S. cerevisiae*. The accuracy of the inferred network was examd. by the agreement of our results with the cumulative results of exptl. studies.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 152 OF 169 CAPLUS COPYRIGHT 2005 ACS on  
STN

AN 2002:181162 CAPLUS

DN 137:135903

TI DNA repair capacity after .gamma.-irradiation and  
\*\*\*expression\*\*\* \*\*\*profiles\*\*\* of DNA repair genes in  
resting and proliferating human peripheral blood lymphocytes  
AU Mayer, Claudia; Popanda, Odilia; Zelezny, Otto; von Brevern,  
Marie-Charlotte; Bach, Alfred; Bartsch, Helmut; Schmezer, Peter  
CS Division of Toxicology and Cancer Risk Factors, German  
Cancer Research Center (DKFZ), Heidelberg, 69120, Germany  
SO DNA Repair (2002), 1(3), 237-250 CODEN: DRNEAR; ISSN:  
1568-7864

PB Elsevier Science B.V.

DT Journal

LA English

AB DNA repair plays an important role in maintaining genomic  
integrity, and deficiencies in repair function are known to  
promote cancer development. Several studies have used the  
individual capacity to repair DNA damage in peripheral blood  
lymphocytes (PBLs) as a cancer risk marker. As the cell's ability  
to remove DNA damage may be \*\*\*correlated\*\*\* with  
proliferative activity, it is an important question whether  
quiescent or dividing cells should be used in such studies. The  
aim of our study was to compare DNA repair capacity and  
\*\*\*expression\*\*\* \*\*\*profiles\*\*\* of 70 known DNA repair  
genes, both in resting and phytohemagglutinin (PHA) stimulated  
human PBLs. Using the comet \*\*\*assay\*\*\*, .gamma.-  
radiation-induced DNA damage and repair in lymphocytes was  
analyzed. No difference, either in the rate of radiation-induced  
DNA damage or in DNA repair capacity between PHA-stimulated  
and non-stimulated PBLs was obsd. Stimulated cells, however,  
showed significantly elevated values for background damage.  
Transcriptional profiles of repair genes were analyzed using cDNA  
arrays. Hybridization expts. were performed with mRNA isolated  
from both unstimulated and PHA-stimulated PBLs. More than  
70% of all evaluated genes had const. expression levels. Twelve  
genes responded with a more than two-fold increase of  
transcripts to the mitogenic stimulus. Most of the up-regulated  
repair enzymes are also known to play a role in DNA replication.  
In conclusion, the data presented here suggest that all repair  
proteins needed for the repair of .gamma.-irradn. induced DNA-  
damage, that can be detected by the alk. comet \*\*\*assay\*\*\*,  
are already present in G0 cells at sufficient amts. and do not  
need to be induced once lymphocytes are stimulated to start  
cycling. Our results thus do not support a general increase in  
DNA repair activity of PBLs by PHA stimulation, and the use of  
stimulated PBLs in mol. epidemiol. studies on DNA repair of  
.gamma.-irradn. induced DNA damage seems not to be  
mandatory.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 153 OF 169 CAPLUS COPYRIGHT 2005 ACS on  
STN

AN 2001:856778 CAPLUS

DN 137:382691

TI Genetic differences in hepatic lipid peroxidation potential and  
iron levels in mice

AU Gerhard, Glenn S.; Kaufmann, Elizabeth J.; Wang, Xujun;  
Erikson, Keith M.; Abraham, Joseph; Grundy, Martin; Beard, John  
L.; Chorney, Michael J.

CS Department of Pathology, Penn State College of Medicine,  
Hershey, PA, USA

SO Mechanisms of Ageing and Development (2002), 123(2-3),  
167-176 CODEN: MAGDA3; ISSN: 0047-6374

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

AB Oxidative damage to macromols., including lipids, has been  
hypothesized as a mechanism of aging. One end product of lipid  
peroxidn., malondialdehyde (MDA), is often quantified as a  
measure of oxidative damage to lipids. We used a com.  
colorimetric \*\*\*assay\*\*\* for MDA (Bioxtech LPO-586, Oxis  
International, Portland, OR) to measure lipid peroxidn. potential  
in liver tissue from young (2 mo) male mice from recombinant  
inbred (RI) mouse strains from the C57BL/6J (B6).times.DBA/2J  
(D2) series (BXD). The LPO-586 \*\*\*assay\*\*\* (LPO) reliably  
detected significant differences ( $P < 0.0001$ ) in lipid peroxidn.  
potential between the B6 and D2 parental strains, and yielded a  
more than two-fold variation across the BXD RI strains. In both  
B6 and D2 mice, LPO results were greater in old (23 mo) mice,  
with a larger age-related increase in the D2 strain. As the level  
of iron can influence lipid peroxidn., we also measured hepatic  
non-heme iron levels in the same strains. Although iron level  
exhibited a slightly neg. overall \*\*\*correlation\*\*\* ( $r^2 = 0.119$ )  
with LPO results among the entire group of BXD RI strains, a  
sub-group with lower LPO values were highly \*\*\*correlated\*\*\*  
( $r^2 = 0.704$ ). LPO results were also pos. \*\*\*correlated\*\*\* with  
iron levels from a group of 8 other inbred mouse strains  
( $r^2 = 0.563$ ). The BXD RI LPO data were statistically analyzed to  
nominate quant. trait loci (QTL). A single marker, Zfp4, which  
maps to 55.2 cM on chromosome 8, achieved a significance level  
of  $P < 0.0006$ . At least two potentially relevant candidate genes  
reside close to this chromosomal position. Hepatic lipid peroxidn.  
potential appears to be a strain related trait in mice that is  
amenable to QTL anal.

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE  
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L9 ANSWER 154 OF 169 CAPLUS COPYRIGHT 2005 ACS on  
STN

AN 2001:846330 CAPLUS

DN 136:113125

TI p38 mitogen-activated protein kinase-independent induction  
of gadd45 expression in nerve growth factor-induced apoptosis in  
medulloblastomas

AU Chou, Thomas T.; Trojanowski, John Q.; Lee, Virginia M.-Y.  
CS Center for Neurodegenerative Disease Research, Department  
of Pathology and Laboratory Medicine, University of Pennsylvania  
School of Medicine, Philadelphia, PA, 19104, USA

SO Journal of Biological Chemistry (2001), 276(44), 41120-  
41127 CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB We describe a novel nerve growth factor (NGF)-signaling  
pathway leading to gadd45 induction that is independent of JNK  
and p38 MAPK. We used cDNA arrays representing 588 genes to  
investigate the role of differential gene expression in NGF-  
mediated pleiotropic responses. We compared the \*\*\*gene\*\*\*  
\*\*\*expression\*\*\* \*\*\*profiles\*\*\* obtained from MED283-  
TrkA cells undergoing NGF-induced apoptosis to PC12 cells  
undergoing NGF-induced differentiation. An early and specific

transcriptional target of NGF in MED283-TrkA cells was the DNA-damage-inducible gene gadd45. Its magnitude of induction directly \*\*\*correlated\*\*\* with the magnitude of apoptosis in MED283 clones transfected with mutant TrkA receptors. Although gadd45 has been implicated in stress response signaling, in vitro kinase \*\*\*assays\*\*\* indicated that NGF neither activated c-Jun NH2-terminal kinase (JNK) nor p38 mitogen-activated protein kinase (MAPK). Furthermore, the p38 MAPK inhibitor SB203580 (20 .mu.M) failed to prevent NGF-induced apoptosis and NGF-induced gadd45 expression. These results suggest that differential regulation of gadd45 expression possibly through BRCA1 may be a potential mechanism whereby NGF regulates pleiotropic responses.

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 155 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:723836 CAPLUS

DN 136:3526

TI Seasonally inappropriate body weight induced by food restriction: effect on hypothalamic gene expression in male Siberian hamsters

AU Mercer, Julian G.; Moar, Kim M.; Logie, Tracy J.; Findlay, Patricia A.; Adam, Clare L.; Morgan, Peter J.

CS Aberdeen Centre for Energy Regulation and Obesity, Rowett Research Institute, Aberdeen, AB21 9SB, UK

SO Endocrinology (2001), 142(10), 4173-4181 CODEN:

ENDOAO; ISSN: 0013-7227

PB Endocrine Society

DT Journal

LA English

AB Male Siberian hamsters undergo physiol. wt. change in changing photoperiod. Wt. loss was induced by food restriction in long days to mimic short-day wt. loss, or by food restriction superimposed on short-day wt. loss, to \*\*\*test\*\*\* the hypothesis that the hypothalamus differentiates between wt. change induced by imposed neg. energy balance (inappropriate body wt.) and seasonal, appropriate, body wt. change, even when these are of similar magnitude. Short-day wt. loss was accompanied by reduced POMC and leptin receptor (OB-Rb) mRNA in the arcuate nucleus but elevated cocaine- and amphetamine-regulated transcript. Melanocortin 3-receptor gene expression was reduced in the arcuate nucleus but elevated in the ventromedial nucleus compared with ad libitum-fed long-day controls. Wt. loss in long-day restricted animals generated a \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* typical of neg. energy balance with low cocaine- and amphetamine-regulated transcript mRNA and elevated OB-Rb. Melanocortin 3-receptor mRNA levels were indistinguishable in short-day and long-day food-restricted hamsters. The hypothalamic \*\*\*correlates\*\*\* of food restriction in short days included up-regulated anabolic neuropeptides and increased OB-Rb mRNA. Low plasma leptin is integrated differently in short-day and long-day restricted animals, and seasonally-inappropriate body wt. in either photoperiod engages the compensatory neuropeptide systems involved in the defense of body wt.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 156 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:688793 CAPLUS

DN 136:274173

TI Chipping away at complex behavior:

Transcriptome/phenotype \*\*\*correlations\*\*\* in the mouse brain

AU Carter, T. A.; Del Rio, J. A.; Greenhall, J. A.; Latronica, M. L.; Lockhart, D. J.; Barlow, C.

CS Laboratory of Genetics, The Salk Institute for Biological Studies, La Jolla, CA, 92037, USA

SO Physiology & Behavior (2001), 73(5), 849-857 CODEN: PHBHA4; ISSN: 0031-9384

PB Elsevier Science Inc.

DT Journal

LA English

AB Highly parallel \*\*\*gene\*\*\* \*\*\*expression\*\*\*

\*\*\*profiling\*\*\* has the potential to provide new insight into the mol. mechanisms of complex brain diseases and behavioral traits. We review how \*\*\*gene\*\*\* \*\*\*expression\*\*\*

\*\*\*profiling\*\*\* in various brain regions of inbred mouse strains has been used to identify genes that may contribute to strain-specific phenotypes. New data, which demonstrate the use of \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* in

combination with behavioral \*\*\*testing\*\*\* to identify candidate genes involved in mediating variation in running wheel activity, are also presented. These and other studies suggest that a combination of \*\*\*gene\*\*\* \*\*\*expression\*\*\*

\*\*\*profiling\*\*\* and more traditional genetic approaches, such as quant. trait locus anal., can be used to identify genes responsible for specific neurobehavioral phenotypes.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 157 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:659035 CAPLUS

DN 136:47906

TI Prediction of sensitivity of esophageal tumors to adjuvant chemotherapy by cDNA microarray analysis of \*\*\*gene\*\*\* - \*\*\*expression\*\*\* \*\*\*profiles\*\*\*

AU Kihara, Chikashi; Tsunoda, Tatsuhiko; Tanaka, Toshihiro; Yamana, Hideaki; Furukawa, Yoichi; Ono, Kenji; Kitahara, Osamu; Zembutsu, Hitoshi; Yanagawa, Rempel; Hirata, Koichi; Takagi, Toshihisa; Nakamura, Yusuke

CS Human Genome Center, Institute of Medical Science, University of Tokyo, Tokyo, 108-8639, Japan

SO Cancer Research (2001), 61(17), 6474-6479 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB We applied cDNA microarray analyses of 9216 genes to establish a genetic method for predicting the outcome of adjuvant chemotherapy to esophageal cancers. We analyzed \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of 20 esophageal cancer tissues from patients who were treated with the same adjuvant chemotherapy after removal of tumor by operation, and we attempted to find genes assocd. with the duration of survival after surgery. By comparing \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of those cancer tissues, we identified by statistical anal. 52 genes that were likely to be \*\*\*correlated\*\*\* with prognosis and possibly with sensitivity/resistance to the anticancer drugs. We also developed a drug response score based on the differential expression of these genes, and we found a significant \*\*\*correlation\*\*\* between the drug response score and individual patients' prognoses. Our results indicated that this scoring system, based on microarray anal. of selected genes, is likely to have great



potential for predicting the prognosis of individual cancer patients with the adjuvant chemotherapy.  
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 158 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:605822 CAPLUS  
DN 136:198754  
TI Overexpression of interferon .gamma.-inducible protein 10 in the liver of patients with type I autoimmune hepatitis identified by suppression subtractive hybridization  
AU Nagayama, Kazuyoshi; Enomoto, Nobuyuki; Miyasaka, Yuka; Kurosaki, Masayuki; Chen, Cheng-Hsin; Sakamoto, Naoya; Nakagawa, Mina; Sato, Chifumi; Tazawa, Junichi; Ikeda, Takaaki; Izumi, Namiki; Watanabe, Mamoru  
CS Departments of Gastroenterology and Hepatology and Health Science, Faculty of Medicine, Tokyo Medical and Dental University, Tokyo, Japan  
SO American Journal of Gastroenterology (2001), 96(7), 2211-2217 CODEN: AJGAAR; ISSN: 0002-9270  
PB Elsevier Science Inc.  
DT Journal  
LA English  
AB To clarify \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* in the liver may elucidate the pathogenesis of type I autoimmune hepatitis (AIH). Using suppression subtractive hybridization (SSH), we identified genes overexpressed in the liver of AIH. A small liver biopsy sample from a patient with definite AIH was available to be analyzed in our system. By mixing cDNA synthesized from this sample as a " \*\*\*tester\*\*\* " and cDNA from a normal liver as a "driver," we subtracted cDNA to enrich genes overexpressed in AIH. After polymerase chain reaction (PCR) amplification and subcloning, we identified subtracted genes by sequencing 50 randomly selected clones. Only one cDNA fragment, which is identical to interferon inducible protein 10 (IP-10), was overexpressed by >10 times in the liver of AIH, as compared with control. We confirmed IP-10 overexpression in all eight patients with AIH by reverse transcription PCR. Immunohistochem. anal. demonstrated increased IP-10 expression in hepatocytes in the liver of AIH. Reverse transcription PCR anal. of 63 liver biopsy samples with various liver diseases revealed that IP-10 expression was significantly higher in AIH and chronic hepatitis C than in other liver diseases. Interestingly, the amt. of IP-10 mRNA expression was \*\*\*correlated\*\*\* with serum ALT values in AIH, but not in chronic hepatitis C. These results indicate the IP-10 expression in the liver might be used as a preferential marker of AIH, and that IP-10 has some pathophysiol. roles in the liver damage of AIH.  
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 159 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:596397 CAPLUS  
DN 135:222647  
TI Clustering of Hepatotoxins Based on Mechanism of Toxicity Using \*\*\*Gene\*\*\* \*\*\*Expression\*\*\* \*\*\*Profiles\*\*\*  
AU Waring, Jeffrey F.; Jolly, Robert A.; Ciurlionis, Rita; Lum, Pek Yee; Praestgaard, Jens T.; Morfitt, David C.; Buratto, Bruno; Roberts, Chris; Schadt, Eric; Ulrich, Roger G.  
CS Department of Cellular and Molecular Toxicology, Abbott Laboratories, Abbott Park, IL, 60064-6104, USA

SO Toxicology and Applied Pharmacology (2001), 175(1), 28-42 CODEN: TXAPA9; ISSN: 0041-008X  
PB Academic Press  
DT Journal  
LA English  
AB Microarray technol., which allows one to quantitate the expression of thousands of genes simultaneously, has begun to have a major impact on many different areas of drug discovery and development. The question remains of whether microarray anal. and \*\*\*gene\*\*\* \*\*\*expression\*\*\* signature \*\*\*profiles\*\*\* can be applied to the field of toxicol. To date, there are very few published studies showing the use of microarrays in toxicol. and important questions remain regarding the predictability and accuracy of applying \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* to toxicol. To begin to address these questions, we have treated rats with 15 different known hepatotoxins, including allyl alc., amiodarone, Aroclor 1254, arsenic, carbamazepine, carbon tetrachloride, diethylnitrosamine, DMF, diquat, etoposide, indomethacin, methapyrilene, methotrexate, monocrotaline, and 3-methylcholanthrene. These agents cause a variety of hepatocellular injuries including necrosis, DNA damage, cirrhosis, hypertrophy, and hepatic carcinoma. Gene expression anal. was done on RNA from the livers of treated rats and was compared against vehicle-treated controls. The gene expression results were clustered and compared to the histopathol. findings and clin. chem. values. Our results show strong \*\*\*correlation\*\*\* between the histopathol., clin. chem., and \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* induced by the agents. In addn., genes were identified whose regulation \*\*\*correlated\*\*\* strongly with effects on clin. chem. parameters. Overall, the results suggest that microarray \*\*\*assays\*\*\* may prove to be a highly sensitive technique for safety screening of drug candidates and for the classification of environmental toxins. (c) 2001 Academic Press.  
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 160 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:430723 CAPLUS  
DN 135:150834  
TI Up-regulation of TRPM-2, MMP-7 and ID-1 during sex hormone-induced prostate carcinogenesis in the Noble rat  
AU Ouyang, X. S.; Wang, X.; Lee, D. T. W.; Tsao, S. W.; Wong, Y. C.  
CS Department of Anatomy, Faculty of Medicine, University of Hong Kong, Hong Kong, Peop. Rep. China  
SO Carcinogenesis (2001), 22(6), 965-973 CODEN: CRNGDP; ISSN: 0143-3334  
PB Oxford University Press  
DT Journal  
LA English  
AB Prostate cancer is the most frequently diagnosed malignancy in the Western world and changes in the ratio of \*\*\*testosterone\*\*\* and estrogens with advancing age is one of the potential risk factors in the development of this disease. However, the mol. mechanisms assocd. with hormone imbalance in prostate carcinogenesis are poorly understood. In this study we induced a high incidence of prostate hyperplasia, dysplasia and adenocarcinoma in the Noble rat using a combination of \*\*\*testosterone\*\*\* and estradiol-17.beta.. Using this animal model, we studied the \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profile\*\*\* during sex hormone-induced prostate carcinogenesis using a cDNA array technique; the results were

further confirmed by RT-PCR, western blotting and immunohistochem. analyses. We found up-regulation of TRPM-2 ( \*\*\*testosterone\*\*\* -repressed prostatic message-2), MMP-7 (matrix metalloproteinase-7) and Id-1 (inhibitor of differentiation or DNA binding) during development of sex hormone-induced prostate cancer. Increased expression of TRPM-2 and MMP-7 was obsd. in both premalignant and malignant tissues after sex hormone treatment, indicating their role in the early stages of hormone response and prostate cancer development. In contrast, Id-1 was expressed at relatively low levels in all premalignant samples but increased in malignant cells, suggesting its potential roles as a biomarker for prostate cancer cells. Furthermore, expression of Id-1 appeared to be stronger in poorly differentiated lesions than in well-differentiated carcinomas, suggesting that the levels of Id-1 expression may be \*\*\*correlated\*\*\* with the malignancy of tumors. Our results provide the first evidence of up-regulation of TRPM-2, MMP-7 and Id-1 during sex hormone-induced prostate carcinogenesis and strongly suggest their assocn. with the development of prostate cancer.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 161 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:382210 CAPLUS

DN 136:49582

TI RNA expression in the early characterization of hepatotoxics in Wistar rats by high-density DNA microarrays  
AU Bulera, Steven J.; Eddy, Susan M.; Ferguson, Erika; Jatko, Timothy A.; Reindel, James F.; Bleavins, Michael R.; De La Iglesia, Felix A.

CS Drug Safety Evaluation, Pfizer Global Research and Development, Ann Arbor, MI, 48105, USA

SO Hepatology (Philadelphia, PA, United States) (2001), 33(5), 1239-1258 CODEN: HPTLD9; ISSN: 0270-9139

PB W. B. Saunders Co.

DT Journal

LA English

AB High-d. microarrays are useful tools to study gene expression for the purpose of characterizing functional tissue changes in response to the action of drugs and chems. To \*\*\*test\*\*\* whether high-d. expression data can identify mechanisms of toxicity and to identify an unknown sample through its RNA expression pattern, groups of male Wistar rats were administered 6 hepatotoxics. The compds. chosen for this study were microcystin-LR (MLR), phenobarbital (PB), lipopolysaccharide (LPS), carbon tetrachloride (CT), thioacetamide (THA), and cyproterone acetate (CPA). These hepatotoxics are known to induce adverse liver effects through different mechanisms. Liver mRNA was isolated and used to generate biotinylated cRNA for hybridization to a custom 1,600-rat gene DNA microarray. Treatment \*\*\*correlation\*\*\* matrixes analyzed hybridization data from a hepatotoxicant-blinded sample, with gene expression coeffs. (GEC) evaluated by means of hierarchical cluster anal. and visual representation as dendrograms. The exptl. liver toxicity from the different treatments was confirmed by means of concurrent histopathol., liver enzymes, and bilirubin \*\*\*assays\*\*\*. This toxicogenomic anal. identified multiple genes and groups of genes that were affected by the hepatotoxics on study, indicating that high-d. microarray expression data are useful to identify groups of genes involved in toxicity. In addn., the mRNA \*\*\*expression\*\*\* \*\*\*profile\*\*\* of an unidentified sample can be accurately identified when compared with the

\*\*\*expression\*\*\* \*\*\*profiles\*\*\* resident in the data set.

This study supports the use of \*\*\*gene\*\*\*

\*\*\*expression\*\*\* - \*\*\*profiling\*\*\* technol. to det. or to predict toxic liver effects.

RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 162 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:199221 CAPLUS

TI Structure-based datamining software for \*\*\*correlating\*\*\* compound classes and gene expression

AU Blower, Paul E.; Yang, Chihae

CS LeadScope, Inc, Columbus, OH, 43212, USA

SO Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, 2001 (2001) CINF-064 CODEN: 69FZD4

PB American Chemical Society

DT Journal; Meeting Abstract

LA English

AB The National Cancer Institute routinely \*\*\*tests\*\*\* the growth inhibition and cytotoxicity of compds. against a panel of 60 human cancer cell lines (NCI60). To date more than 70,000 compds. have been \*\*\*tested\*\*\*. Recently, researchers at the NCI and their collaborators published a study in which they used cDNA microarrays to generate \*\*\*gene\*\*\*

\*\*\*expression\*\*\* \*\*\*profiles\*\*\* for the NCI60 and then used bioinformatics techniques to \*\*\*correlate\*\*\* those profiles with drug activity patterns of \*\*\*tested\*\*\* compds. We have developed structure-based datamining and visualization software that can assist researchers in exploring this rich data set. In this talk, we will describe statistical techniques used to select genes with characteristic expression patterns and illustrate how we used the software to identify several compds. classes that are well- \*\*\*correlated\*\*\* with the expression patterns of selected genes.

L9 ANSWER 163 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:20542 CAPLUS

DN 134:216941

TI Understanding and exploiting the mechanistic basis for selectivity of polyketide inhibitors of F0F1-ATPase

AU Salomon, Arthur R.; Voehringer, David W.; Herzenberg, Leonard A.; Khosla, Chaitan

CS Department of Chemistry and Chemical Engineering, Stanford University, Stanford, CA, 94305, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2000), 97(26), 14766-14771 CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Recently, a family of polyketide inhibitors of F0F1-ATPase, including apoptolidin, ossamycin, and oligomycin, were shown to be among the top 0.1% most cell line selective cytotoxic agents of 37,000 mols. \*\*\*tested\*\*\* against the 60 human cancer cell lines of the National Cancer Institute. Many cancer cells maintain a high level of anaerobic carbon metab. even in the presence of oxygen, a phenomenon that is historically known as the Warburg effect. A mechanism-based strategy to sensitize such cells to this class of potent small mol. cytotoxic agents is presented. These natural products inhibit oxidative phosphorylation by targeting the mitochondrial F0F1 ATP synthase. Evaluation of \*\*\*gene\*\*\* \*\*\*expression\*\*\*

\*\*\*profiles\*\*\* in a panel of leukemias revealed a strong \*\*\*correlation\*\*\* between the expression level of the gene encoding subunit 6 of the mitochondrial FOF1 ATP synthase (known to be the binding site of members of this class of macrolides) and their sensitivity to these natural products. Within the same set of leukemia cell lines, comparably strong drug-gene \*\*\*correlations\*\*\* were also obsd. for the genes encoding two key enzymes involved in central carbon metab., pyruvate kinase, and aspartate aminotransferase. The authors propose a simple model in which the mitochondrial apoptotic pathway is activated in response to a shift in balance between aerobic and anaerobic ATP biosynthesis. Inhibitors of both lactate formation and carbon flux through the Embden-Meyerhof pathway significantly sensitized apoptolidin-resistant tumors to this drug. Nine different cell lines derived from human leukemias and melanomas, and colon, renal, central nervous system, and ovarian tumors are also sensitized to killing by apoptolidin.  
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 164 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:3213 CAPLUS  
DN 135:74810  
TI \*\*\*Gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* of primary breast carcinomas using arrays of candidate genes  
AU Bertucci, Francois; Houlgatte, Remi; Benziane, Athmane; Granjeaud, Samuel; Adelaide, Jose; Tagett, Rebecca; Loriod, Beatrice; Jacquemier, Jocelyne; Viens, Patrice; Jordan, Bertrand; Birnbaum, Daniel; Nguyen, Catherine  
CS Laboratoire de Biologie des Tumeurs, TAGC, Institut Paoli-Calmettes (IPC), Marseille, Fr.  
SO Human Molecular Genetics (2000), 9(20), 2981-2991  
CODEN: HMGEES; ISSN: 0964-6906  
PB Oxford University Press  
DT Journal  
LA English  
AB Breast cancer is characterized by an important histoclin. heterogeneity that currently hampers the selection of the most appropriate treatment for each case. This problem could be solved by the identification of new parameters that better predict the natural history of the disease and its sensitivity to treatment. A large-scale mol. characterization of breast cancer could help in this context. Using cDNA arrays, we studied the quant. mRNA expression levels of 176 candidate genes in 34 primary breast carcinomas along three directions: comparison of tumor samples, \*\*\*correlations\*\*\* of mol. data with conventional histoclin. prognostic features and gene \*\*\*correlations\*\*\*. The study evidenced extensive heterogeneity of breast tumors at the transcriptional level. A hierarchical clustering algorithm identified two molecularly distinct subgroups of tumors characterized by a different clin. outcome after chemotherapy. This outcome could not have been predicted by the commonly used histoclin. parameters. No \*\*\*correlation\*\*\* was found with the age of patients, tumor size, histol. type and grade. However, expression of genes was differential in tumors with lymph node metastasis and according to the estrogen receptor status; ERBB2 expression was strongly \*\*\*correlated\*\*\* with the lymph node status ( $P < 0.0001$ ) and that of GATA3 with the presence of estrogen receptors ( $P < 0.001$ ). Thus, our results identified new ways to group tumors according to outcome and new potential targets of carcinogenesis. They show that the systematic use of cDNA array \*\*\*testing\*\*\* holds great promise to improve the classification of breast cancer in terms of prognosis and

chemosensitivity and to provide new potential therapeutic targets.  
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 165 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2000:801137 CAPLUS  
DN 134:68987  
TI Hox genes and morphological identity: axial versus lateral patterning in the vertebrate mesoderm  
AU Nowicki, Julie L.; Burke, Ann C.  
CS Department of Biology, University of North Carolina, Chapel Hill, NC, 27599, USA  
SO Development (Cambridge, United Kingdom) (2000), 127(19), 4265-4275 CODEN: DEVPED; ISSN: 0950-1991  
PB Company of Biologists Ltd.  
DT Journal  
LA English  
AB The successful organization of the vertebrate body requires that local information in the embryo be translated into a functional, global pattern. Somite cells form the bulk of the musculoskeletal system. Heterotopic transplants of segmental plate along the axis from quail to chick were performed to \*\*\*test\*\*\* the \*\*\*correlation\*\*\* between autonomous morphol. \*\*\*patterning\*\*\* and Hox \*\*\*gene\*\*\* \*\*\*expression\*\*\* in somite subpopulations. The data presented strengthen the \*\*\*correlation\*\*\* of Hox gene expression with axial specification and focus on the significance of Hox genes in specific derivs. of the somites. The authors have defined two anatomical compartments of the body based on the embryonic origin of the cells making up contributing structures: the dorsal compartment, formed from purely somitic cell populations; and the ventral compartment comprising cells from somites and lateral plate. The boundary between these anatomical compartments is termed the somitic frontier. Somitic tissue transplanted between axial levels retains both original Hox expression and morphol. identity in the dorsal compartment. In contrast, migrating lateral somitic cells crossing the somitic frontier do not maintain donor Hox expression but apparently adopt the Hox expression of the lateral plate and participate in the morphol. appropriate to the host level. Dorsal and ventral compartments, as defined here, have relevance for exptl. manipulations that influence somite cell behavior. The \*\*\*correlation\*\*\* of Hox \*\*\*expression\*\*\* \*\*\*profiles\*\*\* and patterning behavior of cells in these two compartments supports the hypothesis of independent Hox codes in paraxial and lateral plate mesoderm.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 166 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2000:364167 CAPLUS  
DN 133:162460  
TI Identification of a novel aspartic-like protease differentially expressed in human breast cancer cell lines  
AU Xin, H.; Stephans, J. C.; Duan, X.; Harrowe, G.; Kim, E.; Grieshammer, U.; Kingsley, C.; Giese, K.  
CS Chiron Corporation, Emeryville, CA, 94608, USA  
SO Biochimica et Biophysica Acta, Molecular Basis of Disease (2000), 1501(2-3), 125-137 CODEN: BBADEX; ISSN: 0925-4439  
PB Elsevier B.V.  
DT Journal

LA English

AB Four different human breast cancer cell lines were examd. to search for genes assocd. with tumor growth and metastasis. Each of these cell lines, MDA-MB-453, MCF-7, MDA-MB-231 and MDA-MB-435, displays different phenotypic characteristics ranging from poorly to highly tumorigenic and metastatic. The differences in \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiles\*\*\* of these cell lines generated by differential display technique should allow one to identify candidates as putative oncogenes or tumor/metastasis suppressor genes. A novel cDNA expressed in the highly tumorigenic and metastatic cell line, MDA-MB-435, was identified and isolated by this approach. The function for this gene, designated ALP56 (aspartic-like protease 56 kDa), in tumor progression is suggested by the homol. of the encoded protein to aspartic proteases, such as cathepsin D. The amino acid residues in two catalytic domains of this family are highly conserved in those domains of ALP56. Northern hybridization indicated that the expression of ALP56 is assocd. with growth and metastasis of MDA-MB-435 tumors in immunodeficient mice. In situ hybridization of biopsies from breast cancer and colon cancer patients indicated that ALP56 is upregulated in human primary tumors and liver metastasis. These results suggest that this novel gene \*\*\*correlates\*\*\* with human tumor progression. RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 167 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:257007 CAPLUS

DN 133:218219

TI Microarray-based \*\*\*expression\*\*\* \*\*\*profiling\*\*\* in prostate tumors

AU Elek, Jacki; Park, Ki Ho; Narayanan, Ramaswamy

CS Center for Molecular Biology and Biotechnology and Department of Biology, Florida Atlantic University, Boca Raton, FL, 33431, USA

SO In Vivo (2000), 14(1), 173-182 CODEN: IVIVE4; ISSN: 0258-851X

PB International Institute of Anticancer Research

DT Journal

LA English

AB High throughput \*\*\*gene\*\*\* \*\*\*expression\*\*\* \*\*\*profiling\*\*\* is increasingly becoming a desirable method for identifying genes differentially expressed in disease vs. normal tissues. Microarrays and gene chips contg. hundreds to thousands of genes of interest, both known and novel, can be used to establish the \*\*\*expression\*\*\* \*\*\*profile\*\*\* of numerous genes in a single expt. In order to validate the hits emerging out of such an expt. it is necessary to use an appropriate panel of the cDNA repository. The authors investigated the usefulness of such a method to identify prostate cancer-specific genes. A microarray contg. 588 known genes was analyzed using cDNA probes derived from normal and three independent prostate tumors. At least 19/588 genes were found to be differentially expressed in the tumors in comparison to the normal tissue. Among the nine \*\*\*test\*\*\* genes chosen, one gene, Glutathione-S-transferase theta 1 (GSTT1), showed a \*\*\*correlation\*\*\* with the microarray results when analyzed by RT-PCR. Using a comprehensive panel of normal and tumor tissues and cancer-derived cell lines, the authors have rapidly validated the expression relevance of GSTT1 in solid tumors. The microarray was also useful in the preliminary identification of androgen-regulated genes in the prostate tumor models. These results indicate that microarray in combination with a relevant

cDNA repository can facilitate rapid identification of potential targets for therapy and diagnosis of prostate and other cancers. RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 168 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:564640 CAPLUS

DN 125:217848

TI Characterization of ovine SRY transcript and developmental expression of genes involved in sexual differentiation

AU Payen, Emmanuel; Pailhoux, Eric; Merhi, Raghida Abou; Gianquinto, Laurence; Kirszenbaum, Marek; Locatelli, Alain; Cotinot, Corinne

CS Laboratoire de Biologie Cellulaire et Moléculaire, INRA, Jouy-en-Josas, 78350, Fr.

SO International Journal of Developmental Biology (1996), 40(3), 567-575 CODEN: IJDBE5; ISSN: 0214-6282

PB University of the Basque Country Press

DT Journal

LA English

AB In mammals, the presence of SRY, the sex-detg. gene located on the Y chromosome is required to induce the gonadal anlage to differentiate as a \*\*\*testis\*\*\*, whereas its absence leads to the development of an ovary. The authors report here the characterization by 5' and 3' RACE anal. of several SRY transcripts which are expressed in the ovine male developing gonads. These transcripts were not detected in any other fetal tissues and were expressed only in the genital portion of the urogenital ridge. The temporal profile of SRY expression analyzed by RT-PCR suggests that in the sheep fetus the role of SRY is not limited to initiating Sertoli cell differentiation as in mice. Indeed, SRY transcripts persist after the full differentiation of the \*\*\*testis\*\*\*. In addn. to SRY, other genes are known to be involved in mammalian sex detn.: Wilms' tumor gene WT-1, steroidogenic factor gene Ftz-F1 (SF-1) and anti-Müllerian hormone (AMH). The authors investigated the expression patterns of these genes by RT-PCR during fetal development in sheep gonads. Concerning WT-1 and SF-1, these results are consistent with those described in mice where the earliest expression was detected before the sexual differentiation in both sexes. In male, the ontogenesis of AMH transcription corresponds to the seminiferous cords formation (30 dpc). In female, the authors have obsd. the presence of SF-1 transcripts from the undifferentiated stage until birth. In addn., P 450 aromatase expression is detected from 30 dpc and is \*\*\*correlated\*\*\* with the presence of 17-ss estradiol in sheep ovary. These data reveal significant differences between rodent and ruminant models concerning the sex-detg. pathway.

L9 ANSWER 169 OF 169 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1990:608632 CAPLUS

DN 113:208632

TI Developmental regulation of metallothionein mRNA, zinc and copper levels in rainbow trout, Salmo gairdneri

AU Olsson, Per Eric; Zafarullah, Muhammad; Foster, Randy; Hamor, Thomas; Gedamu, Lashitew

CS Dep. Biol. Sci., Univ. Calgary, Calgary, AB, T2N 1N4, Can. SO European Journal of Biochemistry (1990), 193(1), 229-35 CODEN: EJBAC1; ISSN: 0014-2956

DT Journal

LA English

AB The metallothionein (MT) \*\*\*gene\*\*\*

\*\*\*expression\*\*\* \*\*\*profile\*\*\* was followed in rainbow

trout during early embryo development and in liver and gonads during the period of sexual maturation. The hepatic MT mRNA levels increase at the end of sexual maturation in both male and female rainbow trout. Although both isoforms of MT mRNA accumulate in the liver, there is a preferential increase in MT-A in the female liver. Concomitantly with this increase in MT there is a redistribution of zinc and copper to MT. In the juvenile female there is an abundance of MT mRNA in the ovaries. This is \*\*\*correlated\*\*\* to high levels of zinc in the MT fraction upon Sephadex G-75 chromatog. During ovary development the MT mRNA levels and the MT-bound zinc levels drop, with an increase in zinc being bound to high-mol.-mass proteins. At ovulation most of the zinc is found in the membrane portion upon centrifugation. In contrast to the ovaries, there are no apparent changes in either trace-metal distribution or MT mRNA levels during \*\*\*testis\*\*\* development. In the developing embryo there is an increase in MT-bound copper at gastrulation. This is accompanied by an increase in both isoforms of MT mRNA. At hatch both the copper and zinc levels increase in the MT fraction, with a concomitant increase in mainly MT-A mRNA. These findings indicate that the variations in MT mRNA levels during development are closely assocd. with metal regulation.

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FILE 'CAPLUS' ENTERED AT 15:41:09 ON 19 SEP 2005

L1 23977 S ((GENE#(W)EXPRESS?)(5A)(PROFIL? OR PATTERN?))/BI,AB

L2 977001 S CORRELAT?/BI,AB

L3 2425 S L1 AND L2

L4 2208064 S (TEST? OR ASSAY?)/BI,AB

L5 539 S L3 AND L4

L6 24135 S (EXPRESSION(W)PROFIL?)/BI,AB

L7 442 S L5 AND L6

L8 320 S L7 NOT 2005/PY

L9 169 S L8 NOT 2004/PY

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